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01 BEFORE THE SCIENTIFIC REVIEW PANEL
01
02 ON TOXIC AIR CONTAMINANTS
02
03 AIR RESOURCES BOARD
03
04 DR. JOHN FROINES, CHAIRMAN
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08 IN THE MATTER OF:)
08)
09 THE AIR RESOURCES)
09 SCIENTIFIC REVIEW PANEL)
10 PUBLIC MEETING)
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15 TRANSCRIPT OF PROCEEDINGS

16

16 LOS ANGELES, CALIFORNIA

17

17 WEDNESDAY, MARCH 11, 1998

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22 REPORTED BY:

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23 TONYA ESPARZA,

23 CSR NO. 11381

24

24 JOB NO.:

25 ARB4858

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01 BEFORE THE SCIENTIFIC REVIEW PANEL

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02 ON TOXIC AIR CONTAMINANTS

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03 AIR RESOURCES BOARD

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DR. JOHN FROINES, CHAIRMAN

IN THE MATTER OF:)
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THE AIR RESOURCES)
SCIENTIFIC REVIEW PANEL)
PUBLIC MEEETING)
_____)

TRANSCRIPT OF PROCEEDINGS,

TAKEN AT SUNSET VILLAGE COVEL COMMONS,

330 DE NEVE DRIVE, UNIVERSITY OF CALIFORNIA,

LOS ANGELES, CALIFORNIA, COMMENCING AT

9:07 A.M., ON WEDNESDAY, MARCH 11, 1998,

HEARD BEFORE JOHN FROINES, CHAIRMAN,

REPORTED BY TONYA ESPARZA, CSR NO. 11381,

A CERTIFIED SHORTHAND REPORTER IN AND FOR

THE STATE OF CALIFORNIA.

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01	APPEARANCES:	
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02	CHAIRMAN:	JOHN FROINES
02		
03	PANEL MEMBERS:	PAUL BLANC
03		GARY FRIEDMAN
04		CRAIG BYUS
04		HANSPETER WITSCHI
05		JAMES SEIBER
05		ANTHONY FUCALORO
06		STANTON GLANTZ
06		PETER KENNEDY
07		
07	OMBUDSMEN:	WILLIAM C. LOCKETT
08		PETER MATTHEWS
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0005

01 LOS ANGELES, CALIFORNIA, WEDNESDAY, MARCH 11, 1998
02 9:07 A.M.
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04

05 DR. FROINES: AS WE GET STARTED, I WANT TO
06 INTRODUCE TWO PEOPLE WHO ARE HERE WHO I BELIEVE ARE
07 IMPORTANT TO THE LONG-TERM PROCESS THAT WE'RE INVOLVED IN
08 WITH RESPECT TO DIESEL EXHAUST.

09 THE FIRST IS BILL FRIEDMAN FROM THE U.C.L.A.
10 SCHOOL OF MEDICINE WHERE HE IS ASSOCIATE DEAN, AND HE IS A
11 MEMBER OF THE BOARD. AND SO HE'S HERE AND WILL BE
12 LISTENING CAREFULLY BECAUSE HE'LL HAVE TO ADDRESS THIS
13 ISSUE COME JULY.

14 AND THE SECOND PERSON I WANTED TO INTRODUCE
15 TO YOU, AND I DON'T SEE HIM, IS MIKE KENNY WHO IS THE
16 EXECUTIVE OFFICER OF THE A.R.B., AND MIKE MUST BE OUT OF
17 THE ROOM. BUT WE'LL GET BACK TO HIM.

18 I -- I WANT TO MAKE A FEW REMARKS AT THE
19 BEGINNING BEFORE I TURN IT OVER TO GEORGE ALEXEEFF, AND
20 I'LL TRY TO MAKE THEM BRIEF, BUT THERE'S A NUMBER OF
21 POINTS I WANT TO COVER.

22 FIRST, I WANT TO WELCOME EVERYBODY WHO IS
23 HERE. THIS IS REALLY A LANDMARK MEETING FOR THE

24 SCIENTIFIC REVIEW PANEL. THE SCIENTIFIC REVIEW PANEL WAS
25 ESTABLISHED IN 1983, AND SINCE THAT TIME, WE HAVE NEVER

0006

01 TAKEN PUBLIC TESTIMONY AT AN S.R.P. MEETING. WE HAVE
02 ALWAYS FELT THAT WE WOULD SUPPORT THE NOTION OF WORKSHOPS
03 AND OTHER GET TOGETHERS, BUT WE HAVE NEVER TAKEN DIRECT
04 PUBLIC TESTIMONY AT A MEETING, AND SO THIS REPRESENTS A
05 FIRST.

06 WE'RE DOING THIS BECAUSE WE THINK THE
07 SCIENTIFIC ISSUES ASSOCIATED WITH DIESEL EXHAUST ARE OF
08 SUCH SIGNIFICANCE THAT IT WAS IN EVERYBODY'S BEST INTEREST
09 TO HOLD A MEETING AND TO HEAR FROM LEADING SCIENTIST WHO'S
10 HAVE CONDUCTED RESEARCH IN THE AREA OF DIESEL EXHAUSTS AND
11 THE HEALTH EFFECTS ASSOCIATED WITH IT.

12 MIKE KENNY JUST WALKED IN, SO HE CAN RAISE
13 HIS HAND -- WAVE HIS HAND SO YOU ALL KNOW THAT HE'S THE
14 EXECUTIVE OFFICER WHO IS HERE.

15 THE SECOND THING IS THAT THERE WERE A NUMBER
16 OF AFFECTED PARTIES WHO FELT THAT IT WAS IMPORTANT FOR THE
17 PANEL TO HEAR RESPECTED SCIENTISTS; FOR EXAMPLE,
18 JOE MAUDERLY AND ERIC GARSHICK AND OTHERS WHOSE POINTS OF
19 VIEW THEY FELT WERE IMPORTANT TO HAVE HEARD BY THE PANEL
20 IN A DIRECT FASHION. AND SO WE'VE ATTEMPTED TO BE
21 RESPONSIVE.

22 IN GENERAL, THIS ISSUE HAS RAISED KEEN
23 INDUSTRY IN THE COMMUNITY AT LARGE, AND SO WE ALL FELT
24 THAT IT WOULD BE BEST SERVED IF WE HAD A MEETING LIKE
25 THIS, BREAKING OUR TRADITIONAL POLICY AND GETTING INPUT --

0007

01 THE BEST POSSIBLE INPUT WE COULD AS THIS PROCESS MOVED
02 FORWARD. CLEARLY, IT'S AN ISSUE OF CONSIDERABLE CONCERN
03 AND MAGNITUDE.

04 SO WHETHER WE HAVE THESE IN THE FUTURE WILL
05 IN SOME PARTS DEPEND ON HOW WELL WE DO TODAY, BUT AT LEAST
06 WE'RE GOING TO TAKE A SHOT AT HAVING A MEETING IN WHICH WE
07 HAVE STRONG SCIENTIFIC INPUT TO -- TO THE PANEL.

08 AND -- AND I SHOULD SAY AT THE OUTSET THAT
09 THE INPUT TO THE PANEL TODAY WILL BE LIMITED TO SCIENCE.
10 WE'RE NOT TALKING ABOUT COST BENEFIT, RISK MANAGEMENT,
11 LEGAL ISSUES, ET CETERA, ET CETERA, ET CETERA. WE ARE
12 ONLY GOING TO HEAR FROM PERSONS AROUND ISSUES OF SCIENCE.

13 NOW, THERE ARE SOME LEADING SCIENTISTS WHO
14 WERE NOT ABLE TO ATTEND AND NOT INVITED. AARON COHEN FROM
15 H.E.I. IS NOT HERE, MOOGALVKAR FROM THE UNIVERSITY OF
16 WASHINGTON, ROGER MC CLELLAN FROM C.I.T., AND OTHERS WE
17 COULD NAME. THERE ARE CLEARLY SOME OUTSTANDING SCIENTISTS
18 IN THE COUNTRY WHO WE WOULD HAVE LIKE TO HAVE HAD, BUT FOR
19 THE SAKE OF TIME WE SIMPLY COULDN'T INVITE EVERYBODY. WE
20 WOULD HAVE LIKED TO.

21 I THINK THAT -- SO I'M VERY PLEASED TO
22 WELCOME THE PANEL AND THE SPEAKERS AND THE AUDIENCE WHO
23 WILL BE PARTICIPATING. I THINK WE WILL HEAR SOME -- SOME
24 QUITE NEW INFORMATION FROM SOME OF THE SPEAKERS, AND I
25 THINK THAT'S GOOD AS WE GO THROUGH THE DAY, AND I HOPE

0008

01 THAT WE WILL HEAR NEW INFORMATION THAT WILL ADD TO WHAT WE
02 ALREADY HAVE CONSIDERED, AND I HOPE WILL HAVE SIGNIFICANT

03 DISCUSSION.

04 I'M GOING TO BE TRYING TO BE A PRETTY TOUGH
05 SERGEANT AT ARMS TODAY BECAUSE FOR THIS TO WORK, WE'RE
06 GOING TO HAVE TO STAY ON TRACK, AND THAT'S WHY I EVEN
07 DON'T WANT TO GO ON TOO LONG MYSELF HERE, BUT WE'RE GOING
08 TO ORGANIZE THE DAY AS FOLLOWS: THERE WILL BE NO
09 QUESTIONS AFTER EACH SPEAKER. WE WILL TAKE QUESTIONS
10 AFTER EACH GROUP OF SPEAKERS HAVE SPOKEN. AFTER A GROUP
11 OF SPEAKERS HAS SPOKEN, WE WILL ASK IF EITHER OF THEM, IN
12 THE CASE OF -- FOR EXAMPLE, BARBARA AND JOE, WANT TO
13 COMMENT ON EACH OTHERS PRESENTATIONS.

14 IF THERE ARE NO -- IF THERE ARE NO DISCUSSION
15 OR EXCHANGE AT THAT POINT, THEN WE WILL OPEN IT UP TO
16 QUESTIONS AND ANSWERS IN DISCUSSION FROM THE SCIENTIFIC
17 REVIEW PANEL AND OTHER SPEAKERS.

18 SO THERE WILL BE -- ATTEMPT TO BE A DIALOGUE
19 AFTER EACH SESSION OCCURS BETWEEN THE PEOPLE WHO WERE
20 SITTING AT THIS TABLE.

21 IF THERE IS TIME AT THE END OF EACH
22 QUESTION-ANSWER PERIOD, AND THE DISCUSSION HAS -- HAS DIED
23 OUT, THEN I WILL TAKE QUESTIONS FROM THE FLOOR. BUT FOR
24 THE MOST PART, WE WON'T BE TAKING QUESTIONS FROM THE FLOOR
25 UNTIL THERE IS TIME.

0009

01 TOWARDS THE END OF THE DAY, WE'VE ALLOTTED
02 QUITE A BIT OF TIME FOR DISCUSSION, AND TOWARDS THE END OF
03 THE DAY I THINK WE WILL OPEN IT UP FOR MORE DISCUSSION
04 FROM THE FLOOR IN ORDER THAT WE TRY AND HEAR FROM
05 EVERYONE.

06 BUT FOR THE MOST PART, WE'RE GOING TO HAVE
07 DISCUSSION BETWEEN SPEAKERS -- DISCUSSIONS BETWEEN
08 SPEAKERS, PEOPLE WHO ARE SPEAKERS, BUT NOT HAVING GIVEN
09 THEIR TALK AND THE SCIENTIFIC REVIEW PANEL TO HAVE A
10 REASONABLY DISCIPLINED LEVEL OF DISCUSSION.

11 SO THAT -- THAT IS SORT OF THE GROUND RULES
12 FOR TODAY.

13 NOW, THIS -- AT THIS POINT, THIS PANEL HAS
14 NOT FORMALLY TAKEN UP THE DOCUMENT. WE WILL FORMALLY
15 DISCUSS THE DOCUMENT AT OUR MEETING IN APRIL, WHICH IS
16 APRIL 22ND. THE AIR RESOURCES BOARD PRESUMABLY WILL HEAR
17 THE DISCUSSION ABOUT DIESEL IN THEIR MEETING ON JULY 23RD.
18 SO THE PROCESS IS MOVING TO -- TO CLOSURE.

19 I DO WANT TO EMPHASIZE A COUPLE OF POINTS
20 BEFORE TURNING IT OVER TO GEORGE. ONE IS THAT IN CARRYING
21 OUT OUR MANDATE, IT'S IMPORTANT TO REMEMBER THAT THE
22 HEALTH AND SAFETY CODE SECTION 39650(E) OF THE STATE OF
23 CALIFORNIA SPECIFICALLY STATES WHILE ABSOLUTE AND
24 UNDISPUTED SCIENTIFIC EVIDENCE MAY NOT BE AVAILABLE TO
25 DETERMINE THE EXACT NATURE AND EXTENT OF RISKS, IT IS

0010

01 NECESSARY TO TAKE ACTION TO PROTECT PUBLIC HEALTH.

02 WE UNDERSTAND THAT WITH RESPECT TO DIESEL
03 THERE'RE GOING TO BE UNCERTAINTIES. ALL THE SCIENTIFIC
04 ISSUES ARE NOT GOING TO BE RESOLVED IN THIS MEETING WITH
05 THESE DOCUMENTS AND WITH OTHER NEW INPUT THAT OCCURS; AND
06 THAT WE BELIEVE THAT ADDITIONAL RESEARCH IS NECESSARY TO
07 CLARIFY THOSE ISSUES.

08 BUT THAT DOESN'T PREVENT US FROM FINDING A
09 CHEMICAL AS A TOXIC AIR CONTAMINANT, AND IT'S IMPORTANT TO
10 REALIZE THAT -- THAT WE ARE MAKING DECISIONS WITHIN A
11 CONTEXT OF UNCERTAINTY AND RECOGNIZING AND ACKNOWLEDGING
12 UNCERTAINTY, BUT ALSO RECOGNIZING THAT THERE IS A PUBLIC
13 HEALTH NEED TO MAKE DECISIONS. AND SO WITHIN THAT
14 CONTEXT, WE CAN GO FORWARD.

15 IN THAT REGARD, AT SOME LEVEL, WE'RE LOOKING
16 AT ISSUES THAT WE CAN DEFINE ON A QUALITATIVE BASIS. IS
17 DIESEL EXHAUST A LUNG CARCINOGEN? DOES IT PRODUCE
18 NON-RESPIRATORY MORBIDITY AND MORTALITY? ARE THERE
19 IMMUNOLOGIC EFFECTS ASSOCIATED WITH? ARE THERE PRODUCTIVE
20 EFFECTS ASSOCIATED WITH IT? IS THERE GENOTOXICITY?

21 THERE ARE A SERIES OF QUALITATIVE ISSUES THAT
22 I HOPE WE CAN COME TO SOME GENERAL AGREEMENT ON. I THINK
23 IN THE AREA OF QUANTITATIVE RISK ASSESSMENT THERE ARE
24 GOING TO BE DIFFERENCES, THERE ARE GOING TO BE
25 UNCERTAINTIES, AND HOPEFULLY OVER TIME THOSE UNCERTAINTIES
0011 CAN BE RESOLVED.

02 BUT THE FINDING OF A TOXIC AIR CONTAMINANT IS
03 NOT DEPENDENT UPON HAVING THE RISK ASSESSMENT HAVE
04 BE -- SOMETHING OF A GOLD STANDARD. AND I THINK IT'S VERY
05 IMPORTANT TO UNDERSTAND THAT; THAT THE DESIGNATION OF A
06 TOXIC AIR CONTAMINANT DEPENDS UPON OUR FINDING OF
07 SIGNIFICANT HEALTH EFFECTS TO -- TO MAKE THAT DESIGNATION
08 POSSIBLE.

09 THE LAST THING I WANT TO EMPHASIZE, AND I'VE
10 ALREADY SORT OF ALLUDED TO IT, IS THAT WHAT WE'RE TALKING
11 ABOUT HERE TODAY IS LUNG CANCER FOR THE MOST PART, OR THE
12 CARCINOGENESIS OF DIESEL EXHAUST.

13 WE ARE NOT TALKING ABOUT EXCESS BRONCHITIC --
14 BRONCHITIC SYMPTOMS OF COUGH AND PHLEGM. WE'RE NOT
15 TALKING ABOUT WHEEZING, DECREMENTS IN PULMONARY FUNCTION;
16 THAT IS, WE'RE NOT TALKING ABOUT ACUTE AND CHRONIC
17 RESPIRATORY EFFECTS ASSOCIATED WITH DIESEL.

18 WE'RE NOT TALKING ABOUT INFLAMMATORY EFFECTS
19 ASSOCIATED WITH DIESEL EXHAUST EXPOSURE IN ANIMALS, EXCEPT
20 INSOFAR AS JOE ADDRESSES THAT IN RELATIONSHIP TO CANCER.

21 AND WE'RE NOT TALKING SO MUCH ABOUT -- WE
22 WON'T BE TALKING ABOUT REPRODUCTIVE EFFECTS OR IMMUNOLOGIC
23 EFFECTS.

24 IN OTHER WORDS, THERE ARE A SERIES OF AREAS
25 THAT ARE EXTREMELY IMPORTANT AND THAT THIS PANEL HAS TO
0012 REVIEW WITH GREAT CARE BEFORE THE APRIL MEETING; THAT IS,
01 THE NONCANCER EFFECTS SO THAT WE MAKE SURE THAT WE'RE
02 ADDRESSING THE WHOLE PACKAGE AND NOT HAVE THE DEBATE BE --
03 BE -- END UP BEING VERY NARROWLY FOCUSED.

04 SO THOSE ARE THE REMARKS I THOUGHT WERE
05 IMPORTANT TO TRY AND SET SOMETHING OF A CONTEXT FOR THE
06 MEETING, AND NOW WHAT I WOULD LIKE TO DO IS TURN IT OVER
07 TO GEORGE ALEXEEFF WHO CAN GIVE US AN UPDATE ON THE ACTUAL
08 DOCUMENT PREPARATION.

09 GEORGE.

10 DR. ALEXEEFF: GOOD MORNING, EVERYONE. I'M
11 GEORGE ALEXEEFF. AND ON OCTOBER 16TH OF LAST YEAR WE MADE

13 A PRESENTATION TO THE SCIENTIFIC REVIEW PANEL REGARDING
14 SORT OF THE STATUS OF THE DIESEL DOCUMENT. AND AT THAT
15 POINT, WE SUMMARIZED THE COMMENTS THAT HAD BEEN PRESENTED
16 TO US IN WRITTEN FORM FROM A NUMBER OF -- A NUMBER OF
17 INDIVIDUALS ON OUR -- THE MAY '97 DOCUMENT.
18 AND IN -- IN THOSE DISCUSSIONS WE -- WE
19 INDICATED TO THE PANEL WHAT SOME OF THE KEY ISSUES THAT WE
20 FELT WERE -- THAT WERE -- THAT COULD POTENTIALLY AFFECT
21 THE DOCUMENT, AND THEY INCLUDED SOME OF THE ISSUES THAT I
22 THINK WE'LL PROBABLY HEAR TODAY, THOSE FROM LIKE
23 DR. GARSHICK AND DR. CRUMP, IN TERMS OF THE -- THE
24 CARCINOGENICITY OF DIESEL EXHAUST AND THE USE OF
25 PARTICULAR STUDIES ON THE -- FOR THE QUANTITATIVE --
0013
01 HELLO -- FOR THE QUANTITATIVE RISK ASSESSMENT.
02 I'LL JUST BRIEFLY SUMMARIZE IN RESPONSE TO
03 THAT MEETING AND IN RESPONSE TO THE PUBLIC COMMENTS, WE
04 REVISED THE DOCUMENT. AND THE INDICATION IN THE DOCUMENT
05 GENERALLY -- IT STATES IN THE DOCUMENT WHICH SECTIONS WERE
06 REVISED. YOU COULD FIND THOSE.
07 BUT REGARDING THOSE FACTORS THAT AFFECT
08 CARCINOGENICITY, WE DID REVISE THE GENOTOXICITY SECTION
09 AND EXPANDED THE DISCUSSION OF BIOAVAILABILITY, ADDED SOME
10 ADDITIONAL STUDIES THAT WERE AVAILABLE IN LITERATURE OR
11 HAD BEEN BROUGHT TO OUR ATTENTION BY THE COMMENTS
12 REGARDING THE CARCINOGENICITY EFFECTS. WE ADDED SOME
13 ADDITIONAL STUDIES THAT WERE BROUGHT TO OUR ATTENTION
14 BY -- BY DR. MAUDERLY. WE HAD OTHER ADDITIONAL
15 CARCINOGENICITY STUDIES THAT HAD COME UP WITH REGARDS TO
16 INSTALLATION FOR ANIMALS, WE EXPANDED THE DISCUSSION ON
17 POTENTIAL MECHANISM OF ACTION.
18 AND THEN WE ALSO MADE REVISIONS IN OUR -- IN
19 OUR META-ANALYSIS. WE ALSO, IN THE QUANTITATIVE RISK
20 ASSESSMENT, IN RESPONSE TO COMMENTS MADE BY DR. MAUDERLY
21 AND OTHERS, AND IN RESPONSE TO COMMENTS MADE AT -- BY THE
22 SCIENCE PANEL, OUR QUANTITATIVE RISK ASSESSMENT WAS -- WAS
23 REVISED SUCH THAT THE FINAL RANGE OF RISK IS NOT DEPENDENT
24 UPON THE ANIMAL DATA, BUT FOCUSES MORE ON THE HUMAN DATA
25 SINCE THERE IS HUMAN DATA AVAILABLE.
0014
01 AND FINALLY, I WOULD JUST LIKE TO MENTION
02 THAT WE HAVE ADDED ANOTHER APPENDIX, APPENDIX F, WHERE WE
03 KNOW THERE'S BEEN A LOT OF DISCUSSION AND -- REGARDING
04 SORT OF DISAGREEMENTS OR SCIENTIFIC DIFFERENT
05 INTERPRETATIONS, WHICH I'M SURE WE'LL HEAR SOME ABOUT
06 TODAY, REGARDING THE QUANTITATIVE RISK ASSESSMENT OF --
07 ESPECIALLY THE GARSHICK COHORT STUDY.
08 AND TO TRY TO UNDERSTAND WHY PEOPLE WERE --
09 DIFFERENT INVESTIGATORS WERE COMING UP WITH DIFFERENT
10 ANALYSES, WE ADDED AN APPENDIX F WHICH TRIED TO DESCRIBE
11 THE INFLUENCE OF CHANGING ASSUMPTIONS ON -- ON THE RESULTS
12 OF THE ANALYSIS. SO WE HOPE THAT PROVIDES SOME ADDITIONAL
13 INFORMATION TO EVERYONE.
14 AND OUR COMMENT -- THE IN TERMS OF THE
15 PROCESS, OUR COMMENT PERIOD CLOSES ON MARCH 30TH. SO WE
16 WOULD STILL BE ACCEPTING COMMENTS ON THIS PARTICULAR
17 DOCUMENT PRIOR TO THE SCIENTIFIC REVIEW PANEL MEETING.

18 DR. FROINES: SO HAS EVERYBODY GOT THAT, THAT THE
19 COMMENT PERIOD IS CLOSED ON MARCH 30TH. AND I WOULD URGE
20 PEOPLE TO SEND IN COMMENTS; AND OF COURSE, THE TIME IS
21 SHORT, BUT IF YOU HAVE COMMENTS THAT COME OUT OF THIS
22 MEETING, PLEASE GET COMMENTS IN THAT RELATE TO WHAT WAS --
23 WHAT WAS BEING DISCUSSED AT THIS MEETING.
24 I DON'T KNOW WHEN THE TRANSCRIPT WILL BE
25 AVAILABLE. IT IS PROBABLY GOING TO BE LONGER THAN -- THAN
0015
01 YOU NEED. BUT PLEASE KEEP IN MIND THAT THIS -- THIS
02 MEETING IS ALSO COMMENTABLE UPON.
03 WE HAVE ANOTHER MEMBER OF THE BOARD, AIR
04 RESOURCES BOARD, WHO HAS JOINED US WHICH I THINK IS REALLY
05 TERRIFIC. JOE CALHOUN IS SOMEWHERE. HELLO. WELCOME.
06 AND WE'RE -- AND WE'RE DOING VERY WELL.
07 WE'RE AHEAD OF THE GAME SO FAR. IT'S ONLY 9:22. THAT
08 DOESN'T MEAN THAT EVERY SPEAKER CAN NOW JUST ADD A FEW
09 MINUTES ON TO THEIR RESPECTIVE TALKS.
10 SO WHY DON'T WE MOVE AHEAD, AND OUR FIRST
11 SPEAKER OF THE MORNING IS GOING TO BE JOE MAUDERLY WHO'S
12 WITH LOVELACE RESPIRATORY RESEARCH INSTITUTE OF -- OF
13 NEW MEXICO.
14 JOE IS DIRECTOR OF EXTERNAL AFFAIRS. HE'S
15 CHAIR OF THE U.S. E.P.A. CLEAN AIR SCIENCE COMMITTEE OF
16 THE U.S. E.P.A. SCIENCE ADVISORY BOARD, AND HIS RESEARCH
17 FOCUSES PRIMARILY ON PULMONARY TOXICOLOGY. AND HIS NAME
18 IS VERY WELL KNOWN TO ALL OF US IN THE ROOM, AND SO WE
19 WELCOME HIM.
20 DR. MAUDERLY: WELL, THANK YOU. I THINK THIS ONE
21 WILL DO.
22 MY EXPERTISE, TO THE EXTENT THAT THERE IS
23 ANY, LIES IN THE FIELD OF TOXICOLOGY AND A NUMBER OF YEARS
24 SPENT TRYING TO UNDERSTAND THE UTILITY OF ANIMALS, VARIOUS
25 LABORATORY ANIMAL MODELS, FOR PREDICTING
0016
01 PATHOPHYSIOLOGICAL PROCESSES IN HUMANS.
02 STARTING OUT FROM A RESPIRATORY FUNCTION
03 VIEWPOINT AND NOW, A LOT OF THIS EFFORT HAS BEEN FOCUSED
04 ON RESPONSES TO PARTICLES REGARDING DIESEL EXHAUST AND
05 MANY OTHER THINGS.
06 I'M PUTTING THIS SLIDE UP WHILE I'M WARMING
07 UP HERE SO THAT NO ONE WILL MISTAKE MY MESSAGE. THIS IS
08 MY ONLY MESSAGE, AND I'M JUST GOING TO EXPAND ON IT.
09 I APPRECIATE THE OPPORTUNITY TO COME AND TALK
10 TODAY. THE -- THE PURPOSE OF THIS APPARENTLY HAS EVOLVED
11 A BIT. INITIALLY, IT WAS SORT OF TO REVIEW THE BACKGROUND
12 OF THIS INFORMATION.
13 LAST NIGHT, I UNDERSTAND THAT'S NOT THE --
14 THE CASE, THAT I SHOULD RESPOND FOR SUCCINCTLY TO THE
15 PRESENT DRAFT DOCUMENT AND ASSUME THAT YOU ALL HAVE HEARD
16 THE BACKGROUND OF THE ANIMAL STUDIES MANY TIMES, AND I
17 THINK MOST OF YOU HAVE.
18 SO I WON'T DO MUCH MORE THAN PRESENT
19 INFORMATION THAT SUPPORTS MY -- MY PREMISES. THIS
20 INFORMATION IS ALL PUBLISHED IN THE LITERATURE. I'LL SHOW
21 YOU NOTHING THAT IS NOT AT THIS TIME.
22 I SUBMITTED WRITTEN COMMENTS SOME TIME AGO IN

23 THE FORM OF AN EXCERPT FROM A RECENT CHAPTER THAT I WROTE
24 WHICH CONTAINED THIS INFORMATION IN SUMMARY FORM, AND I
25 ASSUME THAT THE S.R.P. HAS RECEIVED THAT WRITTEN SUMMARY.

0017

01 NOW, I THINK THAT I NEED TO MAKE CLEAR
02 WHAT -- WHAT I'M NOT SAYING. IT'S ALWAYS INTERESTING TO
03 HAVE PEOPLE RESPOND TO YOU LATER ON WITH WHAT THEY THOUGHT
04 THEY HEARD YOU SAYING.

05 I'M NOT SAYING THAT I THINK THAT THERE IS NO
06 CANCER RISK FROM DIESEL EXHAUST. THAT SOME LEVEL OF RISK
07 IS CERTAINLY PLAUSIBLE. I DON'T KNOW WHAT THE LEVEL IS.
08 I THINK IT'S CLEAR THAT NONE OF US HAVE THE ABILITY TO
09 ESTIMATE THAT WITH A HIGH LEVEL OF CONFIDENCE. AND IF
10 THAT WAS NOT THE CASE, THEN WE PROBABLY WOULDN'T BE
11 MEETING TODAY.

12 BUT WHAT I AM SAYING IS THAT I THINK THAT
13 WORK THAT A LARGE COMMUNITY OF RESEARCHES IN MANY
14 DIFFERENT COUNTRIES HAVE DONE OVER THE LAST DECADE, HAVE
15 PROGRESSIVELY POINTED TOWARD THE FACT THAT THE RAT LUNG
16 TUMOR RESPONSE TO HIGH CONCENTRATIONS, CHRONIC EXPOSURES
17 TO HIGH CONCENTRATIONS OF DIESEL EXHAUST, SHOULD NOT BE
18 USED TO ESTIMATE HUMAN CANCER RISK AT LOW LEVELS, AND I'LL
19 SHOW YOU THE DATA SUPPORTING FOR THAT.

20 NOW, THAT IS NOT JUST MY OPINION. THERE HAVE
21 BEEN A LONG STRING OF MEETINGS THAT MANY OF YOU HAVE
22 PARTICIPATED IN OVER THE LAST SEVERAL YEARS, AND THIS
23 ISSUE HAS COME OUT.

24 TWO WEEKS FROM NOW THERE WILL BE A MEETING IN
25 WASHINGTON BY THE INTERNATIONAL LIFE SCIENCES INSTITUTE,

0018

01 WHICH IS FOCUSED SPECIFICALLY ON THE PROBLEM OF WHAT DO WE
02 DO WITH THESE RAT RESPONSES BECAUSE THIS IS NOT JUST A
03 DIESEL ISSUE. THIS IS AN ISSUE THAT HAS TO DO WITH A WIDE
04 RANGE OF PARTICULATE MATERIALS WHERE WE FIND OURSELVES IN
05 A DILEMMA, AND THAT DILEMMA IS THAT IF YOU EXPOSE RATS TO
06 HIGH CONCENTRATIONS LONG ENOUGH TO A WIDE RANGE OF
07 MATERIALS, SOME OF WHICH ARE THOUGHT TO HAVE VERY LOW
08 TOXICITY, IF ANY, LUNG TUMORS WILL OCCUR. AND WE'RE
09 TRYING TO UNDERSTAND WHY THAT IS.

10 NOW, OUR UNDERSTANDING IS PROGRESSING, IT'S
11 EVOLVING. WE THINK WE UNDERSTAND WHAT SOME OF THE
12 PRINCIPAL MECHANISMS MIGHT BE. I KNOW A FEW OF YOU WERE
13 AT THE A.C.G.I.H.M.A.K. MEETING IN SEATTLE LAST FRIDAY,
14 AND YOU HEARD SOME REVIEW OF THE MOST RECENT FINDINGS ON
15 THE MECHANISMS BY WHICH THESE THINGS MIGHT OCCUR. AND I
16 CONCUR WITH THE MATERIAL THAT WAS PRESENTED THERE.

17 WELL, LET ME GO THROUGH THEN. MY POINT IS
18 THAT THE RAT LUNG TUMOR RESPONSE AS WE KNOW IT AT THESE
19 HIGH EXPOSURE LEVELS IS NOT A -- A RELIABLE INDICATOR OF
20 HUMAN LUNG CANCER RISK, AND IN FACT, SHOULD NOT BE USED TO
21 DEVELOP QUANTITATIVE RISK ESTIMATES, ESPECIALLY FOR LOW
22 LEVEL ENVIRONMENTAL EXPOSURES.

23 AND I THINK THAT MOST PEOPLE IN THE FIELD
24 FEEL THAT IT'S ALSO NOT AN APPROPRIATE SIGNAL FOR
25 ESTIMATING CANCER RISKS FROM -- FROM THE HIGHER

0019

01 OCCUPATIONAL EXPOSURES THAT MIGHT OCCUR.

02 NOW, I'LL -- I'LL ILLUSTRATE THIS WITH SOME
03 DATA. MY PRINCIPAL POINTS FOR THIS ARE, FIRST OF ALL, IT
04 IS WELL KNOWN THAT AMONG THE SPECIES THAT HAVE BEEN
05 STUDIED SO FAR, THE RAT RESPONSE DOES NOT ACCURATELY
06 PREDICT RESPONSES IN OTHER RODENTS. WE DON'T HAVE
07 INFORMATION FOR NON-RODENT ANIMAL SPECIES FOR LONG-TERM
08 CARCINOGENESIS STUDIES SO WE DON'T KNOW THAT.

09 ALTHOUGH WE DO HAVE INFORMATION FROM OTHER
10 SPECIES ON EXPOSURES LONG ENOUGH THAT WE CAN COMPARE SOME
11 OF THE TISSUE RESPONSES.

12 SECOND, THE EVIDENCE IS OVERWHELMING THAT THE
13 RAT RESPONSE IS NOT DUE TO CHEMICAL CARCINOGENESIS, AND
14 CHEMICAL CARCINOGENESIS CONTINUES, I THINK, TO BE THE MOST
15 PLAUSIBLE CONCERN FOR HUMAN CANCER RISKS.

16 THIRD, THE CELLULAR RESPONSE WHICH SEEMS TO
17 RESULT IN THESE LUNG TUMORS IN THESE SPECIES ARE NOT
18 TYPICAL OF NON-HUMAN PRIMATES, AND THEY ARE NOT TYPICAL
19 OF HUMANS, AND THAT'S AN AREA OF RESEARCH THAT'S GOING ON
20 RIGHT NOW TO DO A MORE INTENSIVE COMPARISON OF THAT.

21 WELL, LET ME ILLUSTRATE SOME OF THESE POINTS
22 THEN.

23 IS IT POSSIBLE TO DIM THE LIGHTS A BIT?
24 BEING A BIOLOGIST, I HAVE TO SHOW SOME
25 HISTOPATHOLOGY BECAUSE I BELIEVE THAT'S TRUTH. AND IT'S
0020 MUCH EASIER TO PORTRAY NUMBERS BLACK ON WHITE, BUT
01 HISTOPATHOLOGY IS WHAT'S REALLY -- CAN WE HAVE THE LIGHTS
02 DIMMED A BIT? IS THAT POSSIBLE? OH, THANK YOU.

03 THIS IS A RAT LUNG AFTER EXPOSURE FOR
04 18 MONTHS, AND THIS IS THE POINT AT WHICH THE TUMOR
05 RESPONSE IS JUST BEGINNING TO BE REFLECTED IN THESE
06 ANIMALS. IT IS A LATE OCCURRING RESPONSE AND ONLY AFTER
07 SIGNIFICANT NONCANCER DISEASE IS ALREADY INDUCED.

08 THIS IS EXPOSURE AFTER EXPOSURE AT
09 7,000 MICROGRAMS PER CUBIC METER, AND IT'S FROM THE
10 STUDY -- THE MAUDERLY ET AL. STUDY THAT'S BEEN QUOTED MOST
11 FREQUENTLY IN THESE DOCUMENTS.

12 AND WHAT WE SEE IS, ALTHOUGH THERE ARE AREAS
13 OF NORMAL LUNG TISSUE AND AIR SACS, THERE ARE THESE FOCI
14 IN WHICH SOMETHING IS CLEARLY GOING WRONG. AND WHAT YOU
15 CAN SEE ARE BOTH COLLECTIONS OF SOOT-LADEN CELLS WHICH ARE
16 THE DARK COLOR, BUT THE THICKENING OF THOSE STRUCTURES IS
17 CELL PROLIFERATION.

18 BY THAT, I MEAN INCREASED CELL DIVISION. THE
19 LINING CELLS OF THESE AIRSPACES AND TERMINAL AIRWAYS ARE
20 DIVIDING AT AN ABNORMALLY HIGH RATE AND STACKING UP, IF
21 YOU WILL. AND SO YOU HAVE MUCH THICKER TISSUES.

22 AND IT IS THIS EPITHELIAL PROLIFERATIVE
23 RESPONSE THAT SEEMS TO BE KEY IN THE ADVENT OF TUMORS AND
24 ALSO THE INTERSPECIES DIFFERENCES.

0021 THIS IS THE LUNG FROM A MOUSE EXPOSED
01 IDENTICALLY, IN THE SAME STUDY, TO THE SAME CONCENTRATION,
02 AT THE SAME TIME. AND IN FACT, MEASUREMENTS HAVE SHOWN
03 THAT THE MICE HAVE JUST AS MUCH MATERIAL IN THE LUNG AS
04 THE RATS, AND THEY DO RESPOND. THERE IS NONCANCER LUNG
05 DISEASE IN THE MICE, ALBEIT NOT NEARLY AS INTENSE AS IN
06

07 THE RATS.

08 BUT THERE IS NOT A TUMOR RESPONSE EXCEPT IN
09 STRAINS THAT ARE GENETICALLY -- ESPECIALLY SENSITIVE TO
10 TUMOR INDUCTION, AND WE DON'T SEE THE SAME KIND OF FOCAL
11 CELL PROLIFERATION GOING ON THAT WE DO IN THE RATS.

12 NOW, ONE CAN TRANSFORM, BECAUSE THIS MAKES US
13 FEEL MORE COMFORTABLE, THE HISTOLOGICAL FINDINGS INTO
14 DATA, AND THIS IS DONE BY VARIOUS CELL ABLING TECHNIQUES
15 TO ATTEMPT TO DETERMINE THE PORTION OF CELLS THAT ARE
16 DIVIDING AT THE TIME. AND AN INCREASE MEANS AN INCREASE
17 DIVISION RATE.

18 WE HAVE RATS AND MICE. WE HAVE CONTROL AND
19 HIGH-LEVEL EXPOSE, AS I JUST SHOWED YOU. THIS IS AT THE
20 SAME TIME PERIOD AS THE SLIDES THAT I SHOWED YOU. AND WE
21 HAVE TWO LOCATIONS, TERMINAL BRONCHIOLES, THE FINAL
22 AIRWAYS BEFORE THE AIR SACS BEGIN, AND IN THE AIR SACS OR
23 ALVEOLI THEMSELVES.

24 AND YOU CAN SEE THAT IN THE EXPOSED RATS WE
25 HAVE QUITE A RESPONSE IN BOTH LOCATIONS, AND WE HAVE MUCH
0022

01 LESS RESPONSE IN THE MICE. PERHAPS A MARGINAL RESPONSE
02 HERE IN THE ALVEOLUS, AND NEITHER OF THESE WOULD BE A
03 SIGNIFICANT RESPONSE.

04 AND SO THAT JUST CONFIRMS IN NUMBERS WHAT WE
05 SEE VISUALLY, AND THAT IS THERE IS QUITE A SPECIES
06 DIFFERENCE IN THE CELL RESPONSE TO PROVOCATION WITH THESE
07 EXPOSURES.

08 NOW, THE -- THE MOST COGENT THEORIES ABOUT
09 THE GENERATION OF THESE TUMORS HAS TO DO WITH THE RATS'
10 OXIDANT DEFENSES, AND THE FACT THAT THESE PARTICLES IN
11 CELLULAR RESPONSES TO THEM CREATE CELLULAR DAMAGE FROM
12 OXYGEN RADICALS OF CELLULAR CYTOLOGICAL DAMAGE, AND IT CAN
13 ALSO BE DAMAGE TO D.N.A.

14 WE HAVE SOME DATA FROM THAT STUDY THAT I'VE
15 JUST BEEN DISCUSSING THAT GOES ALONG WITH THIS.

16 NOW, THIS IS A BIT COMPLICATED. WE HAVE A
17 RATIO HERE OF THE MOUSE RESPONSE OVER THE RAT RESPONSE.
18 SO A RATIO OF 1 MEANS THEY RESPONDED IDENTICALLY --
19 NUMERICALLY IDENTICALLY, AND THIS IS THE 3500 MICROGRAM
20 PER CUBIC METER EXPOSURE LEVEL IN THAT STUDY IN THE
21 7,000.

22 NOW, WE CAN SEE THAT IF WE LOOK AT THE AMOUNT
23 OF SOOT IN THE LUNG, AND THIS IS AFTER 18 MONTHS OF
24 EXPOSURE, AGAIN, THE SAME TIME POINT AS I'VE BEEN SHOWING
25 YOU, WE SEE THAT THE MICE ACTUALLY HAVE, ON A LUNG WEIGHT
0023

01 BASIS, A GREATER AMOUNT MATERIAL IN THE LUNG THAN THE
02 RAT.

03 OF COURSE, THE RAT LUNGS ARE RESPONDING MORE
04 AND THEY WEIGH MORE. BUT BE THAT AS IT MAY, THE MICE DO
05 NOT RESPOND LESS BECAUSE THERE IS LESS MATERIAL
06 ACCUMULATED. THEY ARE OVERLOADED, IF YOU WILL, HAVE
07 CLEARANCE DEFICITS AND ACCUMULATION OF MATERIAL.

08 BUT IF WE LOOK AT THE NEUTROPHILS, A CELL
09 THAT INDICATES AN INFLAMMATORY RESPONSE, WE SEE THAT THE
10 INFLAMMATORY RESPONSE OF THE MICE IS ONLY ONE-THIRD THAT
11 OF THE RATS.

12 IF WE LOOK DOWN AT THE GLUTATHIONE
13 PARAMETERS, AND GLUTATHIONE IS ONE OF THE KEY ANTI-OXIDANT
14 DEFENSES, WE FIND THE MICE MUCH BETTER EQUIPPED TO HANDLE
15 THIS. THE AMOUNT GLUTATHIONE REDUCTASE AND REDUCED
16 GLUTATHIONE IN THE LUNGS OF THE MICE IS MUCH GREATER THAN
17 IN THE LUNGS OF THE RATS. AND SO THAT'S CONSISTENT WITH
18 THE OXIDANT PATHWAY OF BEING SOME PART OF THIS PICTURE.
19 THIS IS THE TUMOR RESPONSE FROM THAT STUDY,
20 AT THE END OF THE STUDY, AND MANY OF YOU ARE FAMILIAR
21 THESE DATA. THE NUMBERS IN PARENTHESES ARE THE MEDIAN
22 LIFE SPAN IN MONTHS, AND I JUST PORTRAY THAT TO SHOW THAT
23 A SHORTENED LIFE SPAN WAS NOT RESPONSIBLE FOR THE LACK OF
24 RESPONSE IN THE MICE. THERE WAS NOT A SHORTENED LIFE SPAN
25 AT THE HIGH LEVEL COMPARED TO THE CONTROLS.

0024

01 THERE IS A RESPONSE, A TUMOR RESPONSE IN THE
02 RATS, AND THERE'S NOT A TUMOR RESPONSE IN THE MICE.
03 NOW, THAT'S WELL KNOWN. THAT'S BEEN REPEATED
04 ON FOUR CONTINENTS AND SEVERAL LABORATORIES REPEATEDLY IN
05 DIFFERENT STUDIES. THAT SPECIES DIFFERENCE IS WELL KNOWN.
06 AND IT'S ALSO WELL KNOWN THAT IN THE SEVERAL STUDIES THAT
07 HAVE BEEN DONE IN SYRIAN HAMSTERS, NO TUMORS OCCUR.
08 SOME INCREASES IN TUMORS HAVE BEEN OBSERVED
09 IN SOME GROUPS OF STRAIN A OR SINCAR MICE THAT HAVE HIGH
10 BACKGROUND TUMOR LEVELS AND ARE ESPECIALLY SENSITIVE TO
11 TUMOR INDUCTION, BUT THOSE DATA ARE NOT CONSISTENT AMONG
12 THEMSELVES. BUT AMONG WHAT ONE MIGHT CALL A MORE TYPICAL
13 LABORATORY MOUSE THERE IS NO CONSISTENT RESPONSE.
14 SO -- SO THAT HAS TO DO WITH THE FIRST POINT,
15 AND THAT IS THE RAT RESPONSE DOES NOT PREDICT THE RESPONSE
16 IN OTHER RODENTS.
17 THE RAT LUNG EPITHELIUM IS DIFFERENT FROM
18 THAT OF OTHER RODENTS, AND WE BELIEVE -- AND THERE'S
19 GROWING EVIDENCE THAT IT'S DIFFERENT FROM THAT IN HUMANS
20 IN TERMS OF ITS RESPONSE TO HEAVY PARTICLE LOADING. THIS
21 IS JUST ONE INDICATOR.
22 THIS LARGE LESION HAS BEEN ARGUED AS TO
23 WHETHER IT MIGHT BE A BENIGN TUMOR OR NOT. IT'S A
24 SQUAMOUS CYST. IT'S A LARGE POCKET OF KERATIN THAT'S BEEN
25 SECRETED BY CELLS. AND REGARDLESS OF WHETHER OR NOT SOME

0025

01 GROUPS INITIALLY CALLED THIS A TUMOR, ALL GROUPS AROUND
02 THE WORLD AGREE THAT IT HAS NO PARALLEL IN HUMANS, SHOULD
03 NOT BE USED TO COUNT, IF ONE IS GOING TO CALCULATE HUMAN
04 RISK.

05 AND THERE'S ONLY BEEN ONE SUCH LESION THAT'S
06 BEEN IDENTIFIED IN ANOTHER RODENT. WE SAW ONE LESION IN
07 ONE MOUSE OUT OF SEVERAL HUNDRED THAT APPEARED TO HAVE
08 THIS CHARACTERISTIC, ALTHOUGH IT DIDN'T LOOK LIKE THIS
09 SORT OF THING. AGAIN, EVIDENCE THAT IS RAT IS QUITE
10 DIFFERENT.

11 NOW, A NUMBER OF YEARS AGO, IT BEGAN TO BE
12 APPARENT THAT THIS SAME DIFFERENCE AND THIS SAME RESPONSE
13 APPEARED TO BE OCCURRING IN RESPONSE TO SEVERAL
14 PARTICLES.

15 THIS IS NOT A COMPLETE LIST, BUT THIS IS A
16 TABLE FROM A PAPER THAT WAS PUBLISHED LAST FALL COMPARING

17 DIFFERENT ANIMALS' RESPONSES TO INHALED PARTICLES. AND IT
18 JUST SHOWS SEVERAL MATERIALS FOR WHICH THERE IS A POSITIVE
19 TUMOR RESPONSE IN RATS, A NEGATIVE RESPONSE IN MICE, AND A
20 NEGATIVE RESPONSE IN HAMSTERS FOR THOSE MATERIALS THAT
21 HAVE BEEN STUDIED, AND SOME OF THEM HAVE NOT BEEN
22 STUDIED.

23 THAT CAUSED PEOPLE IN THIS FIELD TO BEGIN TO
24 THINK THAT PERHAPS THE ORGANIC FRACTION OF SOOT WAS NOT A
25 PLAYER IN THIS RESPONSE AS WE HAD IMAGINED THAT IT WAS.

0026

01 STUDIES WERE DONE IN TWO LABORATORIES, OURS
02 AND THE FRAUNHOFER (PHONETIC) LABORATORY IN GERMANY, TO
03 COMPARE THE RESPONSE TO EQUAL EXPOSURES TO THE PARTICULATE
04 PHASE OF DIESEL EXHAUST AND TO CARBON BLACK HAVING LITTLE
05 ORGANIC ACTIVITY AND VIRTUALLY NO MUTAGENIC ACTIVITY.

06 I'M FAST FORWARDING TO THE RESULTS. WE HAVE
07 THE LUNG BURDENS; THAT IS THE MILLIGRAMS OF PARTICLES IN
08 THE LUNG, HIGH AND LOW DIESEL, AND THE HIGH DIESEL IN
09 CARBON BLACK WHERE IT'S SIX-AND-A-HALF MILLIGRAMS PER
10 CUBIC METER AIR CONCENTRATION, BELOW AT TWO-AND-A-HALF.

11 BUT IF YOU LOOK AT THE TUMOR RESPONSE, WE SEE
12 THAT ALTHOUGH THERE WAS NEARLY TWICE AS MUCH DIESEL SOOT
13 RETAINED IN THE LUNG AS CARBON BLACK IN TERMS OF
14 MILLIGRAMS, THE TUMOR RESPONSES WERE VERY MUCH THE SAME.

15 IN FACT, IF YOU THINK THE AMOUNT OF MATERIAL
16 IN THE LUNG AT THE END OF EXPOSURE IS AN APPROPRIATE DOSE
17 METRIC, THAT MEANS THE CARCINOGENICITY OF CARBON BLACK WAS
18 QUITE HIGHER THAN DIESEL EXHAUST, BUT CERTAINLY NO
19 INDICATION THAT THE ORGANIC FRACTION OF DIESEL EXHAUST WAS
20 A PLAYER.

21 THIS IS A SUMMARY OF DATA FROM THE OTHER
22 STUDY. IT'S A DIFFERENT PRESENTATION. IT LOOKS AT
23 CUMULATIVE EXPOSURES BECAUSE THE EXPOSURE PATTERNS VARIED
24 FOR THESE MATERIALS, ALTHOUGH THEY WERE ALL CHRONIC
25 BIOASSAYS, AND THE FRAUNHOFER GROUP HAD FOUR DIFFERENT

0027

01 TREATMENT GROUPS WITH DIESEL SOOT.

02 THE LOWEST GROUP DID NOT SHOW A RESPONSE, AND
03 THERE WAS A SLOPE, BUT TITANIUM DIOXIDE AND A CARBON BLACK
04 WERE ON THE SAME SLOPE, INDICATING THEY WERE ON THE SAME
05 DOSE-RESPONSE OR TOXICITY SLOPE. AGAIN, CONFIRMING THAT
06 THE ORGANIC FRACTION DID NOT APPEAR TO BE PLAYING ANY ROLE
07 IN THIS RESPONSE.

08 AND THAT STILL, IN MY VIEW, IS THE MOST
09 PLAUSIBLE REASON FOR CONCERN FOR HUMAN CANCER RISKS.

10 NOW, WE DON'T REALLY CARE ABOUT THESE OTHER
11 RODENTS. WE WANT TO KNOW WHAT THE IMPLICATIONS ARE FOR
12 HUMANS, AND WE'RE WORKING ON THAT.

13 BUT ALONG THE WAY, WE HAVE COMPARED THE RAT
14 LUNG RESPONSE TO THE LUNG RESPONSE OF MONKEYS. THIS IS
15 FROM A STUDY WHICH WAS PERFORMED IN ANOTHER LABORATORY
16 SEVERAL YEARS AGO IN WHICH A CYNOMOLGUS MONKEYS AND RATS
17 WERE EXPOSED IDENTICALLY FOR TWO YEARS.

18 NOW, THAT WAS NOT LONG ENOUGH TO BE A TUMOR
19 BIOASSAY IN THE MONKEYS, AND THE EXPOSURE CONCENTRATIONS
20 WERE LOW ENOUGH THAT IT WAS JUST AT THE MARGIN OF THE
21 RESPONSE FOR THE RATS. BUT IT WAS SUFFICIENT TO COMPARE

22 THE TISSUE RESPONSES. AND THE AIR CONCENTRATIONS WERE
23 2 MILLIGRAMS OR 2,000 MICROGRAMS PER CUBIC METER.
24 THE STUDY ALSO INCLUDED COAL DUST, AND MANY
25 OF YOU ARE FAMILIAR WITH THAT STUDY, AND I'LL JUST GO
0028
01 THROUGH SOME HISTOPATHOLOGY SLIDES BECAUSE AGAIN,
02 REGARDLESS OF THE NUMBERS ONE MIGHT GENERATE, IT IS EASY
03 FOR YOU TO SEE THAT THERE IS QUITE A DIFFERENCE.
04 THIS IS A LARGE AIRWAY CUT IN CROSS SECTION,
05 AND HERE IS DIESEL SOOT COLLECTED. THIS IS A RAT. MOST
06 OF THE MATERIAL IS IN ALVEOLI AND MACROPHAGES, AND YOU CAN
07 SEE THE THICKENING OF THESE CELLS.
08 IN A LARGE AIRWAY OF A MONKEY, THINGS ARE
09 QUITE DIFFERENT. OF COURSE, THE LARGE AIRWAYS HAVE MORE
10 TISSUE IN THERE WALLS. THE MATERIAL TENDS TO COLLECT IN
11 THE INTERSTITIAL LOCATION OR WITHIN THE TISSUE OF THESE
12 AIRWAYS, AND THERE'S VERY LITTLE ALVEOLAR RESPONSE.
13 IF WE GO TO A SMALLER AIRWAY, THIS WOULD BE
14 AN ALVEOLAR DUCT IN THE RAT. AGAIN, WE HAVE THIS TISSUE
15 RESPONSE OUT AN ALVEOLI, AND THE MATERIAL IS PREDOMINANTLY
16 COLLECTED IN THE ALVEOLI.
17 IN THE MONKEY, AGAIN, AT THIS TERMINAL
18 BRONCHIOLAR ALVEOLAR DUCT JUNCTION, WE SEE THE MATERIAL
19 COLLECTED CLOSE TO THE WALLS AND VIRTUALLY NO ALVEOLAR
20 RESPONSE.
21 IF WE LOOK DOWN IN THE AIR SACS, AGAIN, THE
22 RAT RESPONSE, AND AGAIN THESE DATA ARE PUBLISHED AND
23 THESE -- THESE ARE TYPICAL RESPONSES, AND THE MONKEY
24 RESPONSE OR LACK OF RESPONSE.
25 AGAIN, IF YOU DETERMINE THE AMOUNT OF
0029
01 MATERIAL IN THE LUNG, THEY WERE VERY SIMILAR. BUT THE
02 RESPONSES ARE CLEARLY DIFFERENT. NOW, WE DON'T KNOW THE
03 REASON FOR THIS. THERE ARE PEOPLE WORKING ON THAT. WE
04 HAVE SOME IDEAS, BUT THE BOTTOM LINE IS THAT RESPONSES
05 BETWEEN THESE TWO SPECIES ARE MARKEDLY DIFFERENT, AND IT
06 IS THE -- THE DIVISION OF THESE EPITHELIAL OR LINING CELLS
07 THAT GIVES RISE TO THE TUMORS.
08 AND SO THAT SUGGESTS TO US THAT AS IN HUMANS
09 FROM ANECDOTAL DATA FROM PATHOLOGISTS THAT DEAL WITH
10 HEAVILY DUSTED HUMAN LUNGS, THEY DON'T SEE THE KIND OF
11 RESPONSE THAT OCCURS IN THE RAT, AND IN THE MONKEY IT
12 CERTAINLY DOESN'T OCCUR.
13 NOW, I WOULD -- I WOULD LEAVE WITH -- WITH
14 THIS. LET ME SAY THOUGH BEFORE I GO ON TO THIS THAT
15 WHAT'S HAPPENING NOW IS THAT IT ARE A PANEL OF
16 PATHOLOGISTS, AN INTERNATIONAL PANEL OF PATHOLOGISTS.
17 THERE ARE THREE DIFFERENT COUNTRIES INVOLVED AT THIS TIME
18 AND SEVERAL PATHOLOGISTS IN DIFFERENT INSTITUTIONS IN THIS
19 COUNTRY THAT ARE METHODICALLY REVIEWING LUNG MATERIALS
20 FROM BOTH ANIMAL STUDIES AND FROM COLLECTIONS OF HUMAN
21 LUNG MATERIALS TO COMPARE TYPICAL RESPONSES.
22 NOW, OF COURSE, THE EXPOSURES OF HUMANS ARE
23 NOT KNOWN PRECISELY ALTHOUGH THESE ARE FROM OCCUPATIONAL
24 GROUPS WHERE THE PREDOMINANT EXPOSURES ARE KNOWN. AND THE
25 PURPOSE IS NOT TO BE QUANTITATIVE, BUT TO DEVELOP AN
0030

01 UNDERSTANDING AND AGREEMENT AS TO WHETHER OR NOT THE KINDS
02 OF THINGS WE SEE IN RATS AND IN OTHER ANIMALS ARE TYPICAL
03 OF HUMAN LUNGS.

04 WELL, THE FINAL THING I'LL SHOW IS THIS.
05 NOW, THESE ARE THE AGGREGATE DATA FROM EIGHT DIFFERENT
06 STUDIES IN WHICH THERE WERE GROUPS OF RATS THAT WERE LARGE
07 ENOUGH, EXPOSURES LONG ENOUGH, AND SUFFICIENTLY
08 WELL-DOCUMENTED TO BE CONSIDERED ADEQUATE CANCER
09 BIOASSAYS. AND AS MANY OF YOU KNOW, THERE WERE MANY OTHER
10 STUDIES WHICH WERE NOT CONSIDERED ADEQUATE CANCER
11 BIOASSAYS.

12 AND MY POINT IS PRINCIPALLY THIS. THE
13 ABSCISSA IS A WEEKLY CONCENTRATION TIME FACTOR; THAT IS,
14 THE NUMBERS OF HOURS PER DAY THAT THESE ANIMALS WERE
15 EXPOSED, VARIED FROM STUDY TO STUDY. BUT THE SEQUENCE
16 REPEATED ON A WEEKLY BASIS AND THE DATA FROM SEVERAL KINDS
17 OF DATA FIT NICELY WHEN NORMALIZED ON A WEEKLY C TIMES T
18 PRODUCT FOR THE AIR CONCENTRATION DIESEL SOOT.

19 AND THEN THIS IS THE NET TUMOR RESPONSE, THAT
20 IS, THE DASHED LINE INDICATES THE TUMOR RESPONSE OF THE
21 CONTROL GROUP FOR EACH RESPECTIVE STUDY. SO THIS IS THE
22 NET INCREASE IN EACH RESPECTIVE STUDY. THE FILLED CIRCLES
23 ARE GROUPS IN WHICH THERE WAS A STATISTICALLY SIGNIFICANT
24 INCREASE IN LUNG TUMOR INCIDENTS, AND OF COURSE, THE OPEN
25 CIRCLES ARE GROUPS IN WHICH THERE WAS NOT. BUT ALL OF THE

0031 CIRCLES ARE EXPOSED, LIFETIME EXPOSED GROUPS. WELL, NOT
01 LIFETIME. TWO YEARS OR LONGER.

02 NOW, YOU CAN SEE SEVERAL THINGS FROM THIS.
03 FIRST OF ALL, THERE IS A ZONE WHICH EXTENDS BEYOND 100, A
04 FACTOR OF 100, IN WHICH THERE WAS NO RESPONSE OR NO HINT
05 OF A RESPONSE. I'LL COME BACK TO THAT.

06 THEN THERE IS AN AREA OF EXPOSURE IN WHICH
07 THERE ARE BOTH POSITIVE AND NEGATIVE RESULTS. AND THEN
08 THERE'S AN AREA WHERE ALL THE RESULTS ARE POSITIVE. AND
09 YOUR VIEW OF THE SLOPE HERE DEPENDS ON HOW MUCH WEIGHT WE
10 PUT ON THE RESULTS OF THE IWAI STUDY, WHICH HAVE ALWAYS
11 TENDED TO BE SORT OF AN OUTLYER. BUT ASSUMING THAT WE
12 INCLUDE THAT IN, IT'S VERY EASY TO DRAW A DOSE-RESPONSE
13 SLOPE.

14 THE POINT HERE IS THAT THE AIR RESOURCES
15 BOARD CONTINUES TO SPECULATE ABOUT WHETHER OR NOT THERE
16 MIGHT BE AN ORGANIC AFFECT IN THE RATS AT LOW LEVELS. AND
17 THE STUDIES MIGHT NOT BE POWERFUL ENOUGH TO IDENTIFY IT.

18 WELL, IT'S TRUE THAT THESE STUDIES AT THE
19 MOST INVOLVE 200 ANIMALS PER GROUP, AND THAT IS NOT A
20 SUFFICIENTLY ROBUST STUDY TO -- TO DETERMINE THE RISK AT
21 LOW LEVEL.

22 BUT ONE DOESN'T NEED STATISTICAL FITS. I
23 COULD EASILY PUT A STRAIGHT LINE THROUGH HERE AS MANY
24 PEOPLE HAVE, OR I COULD MAKE IT CURVE SLIGHTLY, BUT THESE

0032 DATA SHOW CLEARLY THAT IF ONE LOOKS NOT JUST AT ONE'S
01 STUDY, BUT THE AGGREGATE OF THE DATA THAT WE HAVE
02 AVAILABLE, THERE ARE A LARGE NUMBER OF GROUPS, 10 OF THEM
03 IN FACT, DOWN IN THIS RANGE, IN WHICH THERE IS NO
04 SUGGESTION OF A SLOPE.

06 IF THERE WERE A VISUAL SLOPE HERE, AND IT WAS
07 SIMPLY NOT STATISTICALLY SIGNIFICANT, WE MIGHT FEEL
08 DIFFERENTLY ABOUT IT.

09 BUT IN FACT, THERE IS NO SUGGESTION OF A
10 RESPONSE DOWN IN THIS REGION, AND THIS AIR CONCENTRATION,
11 IF NORMALIZED OVER A 168-HOUR WEEK, WOULD BE
12 595 MICROGRAMS PER CUBIC METER, WHICH IS QUITE HIGH
13 RELEVANT TO ENVIRONMENTAL EXPOSURES.

14 BECAUSE OF THIS AND BECAUSE OF -- OF THE
15 KNOWN FACT THAT THERE HAS TO BE A PROLIFERATIVE NONCANCER
16 LUNG DISEASE RESPONSE BEFORE THE TUMORS APPEAR, IT IS BOTH
17 PLAUSIBLE AND APPARENT THAT THERE IS A THRESHOLD IN THIS
18 EFFECT.

19 AND SO IF WE'RE -- IF WE'RE ESTIMATING LOW
20 LEVEL EFFECTS, WE'RE ESTIMATING IT FROM THIS LEVER OUT
21 HERE AT THESE VERY HIGH EXPOSURE LEVELS, AND IT IS MY
22 POSITION, AND I THINK THAT OF THE COMMUNITY OF PEOPLE
23 DOING THESE STUDIES, IS THAT THAT IS NOT AN APPROPRIATE
24 RESPONSE. THE EVIDENCE IS OVERWHELMING AT THIS POINT THAT
25 IT SHOULD NOT BE USED FOR HUMAN RISK.

0033

01 NOW, WHY WOULD I BOTHER TO SAY THIS? I MEAN,
02 THE CURRENT DOCUMENT DOES NOT USE THE ANIMAL DATA AS PART
03 OF THE FINAL RISK ASSESSMENT. BUT THE POINT IS THAT IT
04 CONTINUES TO CALCULATE RISKS FROM THE RAT DATA AND TO
05 PORTRAY THEM IN TABULAR AND FIGURE FORM. EITHER IT'S
06 USEFUL OR IT'S NOT. AND IF IT'S NOT, THEN WE SHOULDN'T
07 EVEN BE CALCULATING THOSE RISKS FROM THE DATA, AND
08 CERTAINLY NOT USING THEM. ALTHOUGH I THINK THAT
09 CALIFORNIA HAS BEEN VERY RESPONSIVE AND PERCEPTIVE IN NOT
10 RELYING ON THE ANIMAL DATA.

11 SO I'LL QUIT WITH THAT.

12 DR. FROINES: THANK YOU.

13 JUST AS EVERY PANEL OF THIS KIND NEEDS A --
14 JUST A PATHOLOGIST TO DISCUSS THE DATA, AS A TRAINED
15 CHEMIST, OF COURSE, I FEEL THAT EVERY PANEL HAS TO HAVE A
16 CHEMIST, AT LEAST ONE, AND -- IF NOT MORE.

17 OUR NEXT SPEAKER IS BARBARA ZIELINSKA. SHE'S
18 AT THE DESERT RESEARCH INSTITUTE IN RENO, NEVADA, WHICH IS
19 ASSOCIATED WITH THE UNIVERSITY OF NEVADA.

20 SHE IS AN ENVIRONMENT ANALYTICAL CHEMIST AND
21 HAS BEEN LOOKING AT COMPOSITION OF DIESEL EXHAUST AS A
22 RESEARCH MATTER FOR SOME YEARS, AND SO SHE'S GOING TO BE
23 TALKING, I THINK, ABOUT CHEMICAL COMPOSITION OF DIESEL
24 EXHAUSTS AND OTHER RELATED WORK. SO BARBARA ZIELINSKA.

25 DR. ZIELINSKA: GOOD MORNING. CAN YOU HEAR ME

0034

01 GOOD? NO? OH, I'M SORRY. NOW, THAT WILL BE BETTER.

02 OKAY. HOW I CAN SWITCH THIS ON?

03 OKAY. I'M SORRY. I INJURED MY KNEE SOME
04 TIME AGO, AND I HAVE TO USE THIS CRUTCH. SO IT IS A
05 LITTLE BIT UNCOMFORTABLE TO ME.

06 WELL, ACTUALLY THE TITLE OF MY TALK IS THE
07 SUBJECT I WOULD LIKE TO TALK ABOUT. IT'S THE DEVELOPMENT
08 OF THE DIESEL AND GASOLINE VEHICLE CHEMICAL EMISSION
09 PROFILES FOR USE IN THE APPORTIONMENT OF ATMOSPHERIC
10 CARBONACEOUS AEROSOL. AND THIS IS WHAT I'M GOING TO TALK

11 ABOUT.

12 BEFORE I STOP TALKING, I WOULD LIKE TO

13 ACKNOWLEDGE PEOPLE WHO WERE VERY MUCH INVOLVED IN THIS

14 DIFFERENT -- DIFFERENT ASPECTS OF THE STUDY. AND FROM THE

15 DESERT INSTITUTE AND MY COLLEAGUES, DR. ERIC FUJITA AND

16 DR. JOHN SAGEBIEL AND MY GRADUATE STUDENT, TERRY HAYES.

17 AND THE OTHER CONTRIBUTORS, THEY ARE LIKE

18 GENERAL MOTORS, R & D CENTER; S.H. CADLE AND P. MULAWA;

19 COLORADO SCHOOL OF MINES AND COLORADO STATE UNIVERSITY;

20 DOUG LAWSON WHO WAS OUR PROJECT MANAGER FROM THAT STUDY.

21 OUR OBJECTIVES IN THIS TYPE OF STUDIES, IT'S

22 REALLY TO DEVELOP A DISTINCT CHEMICAL EMISSION PROFILES

23 FOR VARIOUS CATEGORIES OF MOTOR VEHICLE, SUCH AS

24 HEAVY-DUTY DIESEL, LIGHT-DUTY GASOLINE, LOW AND HIGH

25 PARTICULATE EMITTING VEHICLE FOR USE IN THE APPORTIONMENT

0035

01 OF ATMOSPHERIC CARBONACEOUS AEROSOL BY CHEMICAL MASS

02 BALANCE.

03 WE ALL PROBABLY KNOW WHAT IS CHEMICAL MASS

04 BALANCE. THIS IS ONE OF THE MOST -- MOST WIDELY USED

05 RECEPTOR MODELS FOR A PORTION OF AMBIENT PARTICLES TO THE

06 SOURCES.

07 THE CHEMICAL MASS BALANCE COMPARE THE

08 CHEMICAL COMPOSITION OF THE SOURCE KNOWN AS THE SOURCE

09 PROFILES, WITH THOSE CHEMICAL COMPOSITIONS OF THE

10 RECEPTORS OF AMBIENT AIR.

11 AND HISTORICALLY, THE CHEMICAL MASS BALANCE

12 USED MOSTLY INORGANIC SPECIES WHICH ARE ELEMENTS, IONS,

13 TOTAL ORGANIC CARBON, TOTAL ELEMENTAL CARBON, THIS TYPE OF

14 SPECIES.

15 HOWEVER, TO DISTINGUISH BETWEEN DIFFERENT

16 KIND OF SOURCES MIGHT BE A LITTLE BIT DIFFICULT JUST BASED

17 ON THIS CONSTITUENTS, CHEMICAL CONSTITUENTS, AND THIS IS

18 ESPECIALLY THE KIND OF CASE FOR MOTOR VEHICLE, TO

19 DISTINGUISH BETWEEN GASOLINE AND DIESEL BASED ON INORGANIC

20 SPECIES ARE VIRTUALLY IMPOSSIBLE BECAUSE THEY ARE SO

21 SIMILAR.

22 WE SAY THAT THE PROFILES ARE COLLINEAR AND WE

23 CAN NOT REALLY DISTINGUISH BETWEEN THAT. THAT'S WHY WE

24 TALKED ABOUT NEW CONSTITUENTS OF CHEMICAL MASS BALANCE OF

25 THE PROFILES, AND THE FIRST THINGS WHICH COMES INTO MIND

0036

01 ARE ORGANIC COMPOUNDS BECAUSE ALL COMBUSTION SOURCES EMIT

02 THOUSANDS AND -- AND HUNDREDS OF THOUSANDS OF ORGANIC

03 COMPOUNDS, AND THERE CERTAINLY HAS TO BE SOME UNIQUE

04 COMPOUNDS WHICH COULD BE USED IN THE CHEMICAL CONSTRUCTION

05 OF THE PROFILES.

06 SO OUR GOAL WAS REALLY TO DEVELOP THE

07 DISTINCT PROFILE TO USING BOTH TRADITIONAL SPECIES, WHICH

08 ARE INORGANIC MOSTLY SPECIES AND ORGANIC COMPOUNDS.

09 WELL, THE QUESTION ALWAYS IS HOW

10 REPRESENTATIVE THE PROFILES ARE. COULD WE EXTRAPOLATE

11 FROM THE SEVERAL DIESEL TO THE WHOLE POPULATION OF DIESEL,

12 FOR SAMPLE, OR FROM SEVERAL CARS TO THE WHOLE POPULATION

13 OF GASOLINE CARS.

14 THIS IS SOME DATA COMPILED CONSERVING THE

15 TRADITIONAL SPECIES ORGANIC AND INORGANIC -- I MEAN, IS

16 MOSTLY ORGANIC AND ELEMENTAL CARBON IN DIFFERENT STUDY
17 WHICH WERE CARRIED OUT AROUND THE COUNTRY.
18 THE FIRST STUDY WERE CARS IN DENVER,
19 COLORADO, WHICH I'M GOING TO TALK A LITTLE MORE LATER.
20 IT'S A STUDY WHICH TESTS AT 15 DIFFERENT DIESEL CARS, AND
21 IT WAS PART OF N.F.R.A.Q.S. STUDY.
22 AND IF YOU LOOK AT THE SPLIT BETWEEN ORGANIC
23 ELEMENT AND CARBON, IT'S VERY DIFFERENT IN DIFFERENT
24 GROUPS OF STUDY. THE ELEMENTAL CARBON COMPOSITION RANGED
25 FROM 75 IN DENVER TO APPROXIMATELY 22 IN PHOENIX. AND THE
0037
01 SAME FOR ORGANIC CARBON IS FROM LIKE 19 IN N.F.R.A.Q.S.
02 THE LOWEST TO 60 IN PHOENIX.
03 NOW, WHAT DOES THE DIFFERENCE MEAN? IS IT A
04 DIFFERENCE HOW THIS STUDY WERE DONE? WELL CERTAINLY.
05 THIS STUDY IN DENVER, COLORADO WERE USING DYNAMOMETER, AND
06 SOME KIND OF A CYCLE. THEN THE STUDY IN LOS ANGELES AND
07 BAKERSFIELD, THEY ALSO USE A DYNAMOMETER. THERE ARE A FEW
08 CARS HERE, BUT THE NUMBERS ARE DIFFERENT.
09 SO IS THERE A DIFFERENCE IN THE AREA? MAYBE
10 THERE IS A DIFFERENT GASOLINE INVOLVED -- I MEAN, A
11 DIFFERENT DIESEL FUEL.
12 THEN THE -- THE STUDY IN PHOENIX DONE BY
13 D.R.I., THEY WERE -- SAMPLING WAS DONE IN THE INSPECTION
14 AND MAINTENANCE STATION. IT MEANS IT WAS A MANY VEHICLE
15 COMBINED TOGETHER IN DIFFERENT SAMPLES.
16 IT'S AGAIN A DIFFERENT -- DIFFERENT TESTING
17 PROCEDURE. IT'S NOT THE FULL CYCLE.
18 SO THIS TYPE OF THINGS MAY HAVE HAD SOME
19 BEARING ON OUR EXHAUST. THIS IS JUST TO SHOW YOU HOW IT
20 LOOKS LIKE, AND IT'S INTERESTING TO ASK IF THIS ELEMENTAL
21 OR ORGANIC CARBON ARE TRUE FOR OTHER CONSTITUENTS, LIKE
22 SOME PARTICULATE ORGANICS.
23 JUST TO COMPARE SOME DIFFERENCES AND TO LOOK
24 AT DIFFERENT AREA AND DIFFERENT MODES OF DOING THE TEST,
25 I'M GOING TO TALK A LITTLE MORE ABOUT THREE DIFFERENT
0038
01 STUDY ONLY.
02 THE FIRST STUDY WAS DONE IN PHOENIX, ARIZONA
03 IN INSPECTION AND MAINTENANCE STATION. AND IT WAS DONE BY
04 US. IT WAS PART OF MY EXPLORATORY GRANT.
05 WE DECIDED TO USE PHOENIX BEFORE BECAUSE
06 ARIZONA HAS CENTRALIZED INSPECTION AND MAINTENANCE
07 PROGRAM. IT MEANS THAT A LOT OF VEHICLES ARE TESTED IN
08 THE RELATIVELY FEW FACILITIES IN THE TOWN.
09 IN CASE OF DIESEL, THEY HAD TWO DIFFERENT
10 FACILITIES, AND WE TESTED -- WE WERE SAMPLING ON THE ROOF
11 ON ONE OF THESE FACILITIES.
12 IN ADDITION, DIESEL AND AUTOS WERE SEPARATE
13 PHYSICALLY IN THOSE FACILITIES. SO WE WERE ABLE TO BE
14 BACK ON THE ROOF AND SAMPLE ONLY DIESEL AND SAMPLE ONLY
15 AUTO. SO THIS WAS HOW IT WAS DONE. IT WAS DONE IN 1995,
16 THE SAMPLING. SO IT WAS RELATIVELY NEW.
17 THE OTHER STUDY I WOULD LIKE TO TALK ABOUT IS
18 DYNAMOMETER TESTS OF IN-USE, IN-SERVICE LIGHT-DUTY
19 GASOLINE VEHICLE DOWN IN NEVADA. IT WAS DOWN IN RENO AND
20 LAS VEGAS, AND THIS WAS PART OF THE REMOTE SENSING STUDY.

21 WHAT IT MEANS WE HAD THE REMOTE SENSOR ON THE
22 ROAD, WHICH WAS MEASURING CO AND HYDROCARBON EMISSION, AND
23 VEHICLE WHICH WERE EMITTING MORE WERE PULL OUT AND GIVEN
24 DYNAMOMETER TEST ON PORTABLE DYNAMOMETER. WE DID IT
25 TOGETHER WITH GENERAL MOTORS AND E.P.A., AND WE MEASURE --
0039 WE COLLECTED SAMPLES AND DO CHEMICAL ANALYSIS FOR THAT.
02 AND THE FINAL IS THE LAST STUDY -- IT'S THE
03 LAST STUDY WHICH DONE LAST WINTER IN DENVER, COLORADO, IN
04 SO-CALLED NORTHERN FRONT RANGE AIR QUALITY STUDY, WHICH
05 WERE -- WHICH MAIN OBJECTIVE WAS REALLY TO APPORTION
06 CARBONACEOUS AEROSOL IN DENVER TO THE DIFFERENT SOURCES,
07 AND HERE I WAS PLANNING CONTRACTOR.
08 AS PART OF THIS STUDY, WE DID A LOT OF SOURCE
09 TESTING JUST TO HAVE A PROFILE FOR DIFFERENT SOURCES.
10 FOR HEAVY-DUTY DIESEL, A COLORADO SCHOOL OF
11 MINE WAS DOING TESTING, AND WE AT D.R.I. WERE DOING
12 ANALYSIS. FOR LIGHT-DUTY VEHICLE, GENERAL MOTOR WAS DOING
13 THIS; HOWEVER, IT IS PART OF STUDIES NOT FINAL YET. SO I
14 CANNOT TALK ABOUT GENERAL MOTOR STUDY.
15 SO I'M GOING TO USE ONLY HEAVY-DUTY DIESEL.
16 JUST FOR IF ANYBODY IS INTERESTED, THIS IS A WEB-PAGE
17 ADDRESS FOR NORTHERN FRONT RANGE AIR QUALITY STUDY. ALL
18 DATA ARE PUBLISHED THERE, WHATEVER IS AVAILABLE. AND I
19 THINK THE WHOLE REPORT FROM HEAVY-DUTY STUDIES IS POSTED
20 ON THE WEB PAGE AS WELL.
21 OKAY. IF -- STARTING FROM THE LAST COLORADO
22 SCHOOL OF MINE TESTING, THIS TABLE SHOWS BRIEFLY WHAT KIND
23 OF A -- OF A VEHICLE WERE TOXIC. THIS IS ALL HEAVY-DUTY
24 DIESEL. THERE WERE 15 OF THEM. THOSE ARE THE SAMPLES
25 WHICH WERE COLLECTED. ACTUALLY THEY TESTED MORE THAN 15,
0040 BUT WE DID ANALYSIS ONLY FOR 15 VEHICLES WHICH WAS
02 SELECTED LIKE THAT. THEY ARE VERY DIFFERENT, BUSES OR
03 GARBAGE TRUCK OR FOR DELIVERY, AND WITH DIFFERENT GROSS
04 VEHICLE WEIGHT AND DIFFERENT ODOMETER MILES.
05 I WOULD LIKE TO -- TO SHOW YOU THE
06 PASSAGES -- SOME OF THE OPACITY DATA WHICH IS REALLY
07 CORRELATED WITH PARTICLE EMISSION, AND THEY ARE VERY
08 DIFFERENT. THEY RANGE FROM LIKE FEW PERCENT UP TO
09 75 PERCENT, THE LAST TRUCK, AND 75 PERCENT IS VERY HIGH.
10 FOR EXAMPLE, IN ARIZONA THE STANDARD IS
11 20 PERCENT. SO THOSE ARE VERY DIFFERENT VEHICLE, VERY
12 DIFFERENT BEHAVIOR.
13 SO IT WAS INTERESTING -- AND THEY WERE ALL
14 TESTED ON DYNAMOMETER USING DIFFERENT CYCLES.
15 THIS IS WEST VIRGINIA, TRUCK CYCLE, CENTRAL
16 BUSINESS DISTRICT, AND HEAVY-DUTY TRANSIT CYCLE. THERE IS
17 NO REALLY OFFICIAL E.P.A. CYCLE LIKE F.T.P. FOR LIGHT
18 DUTY. AND SO THEY WERE USING SOME DIFFERENT WHICH ARE
19 ACCEPTED BY THE COMMUNITY.
20 THIS SLIDE SHOW THE TRADITIONAL MEASURING
21 ELEMENTS, ORGANIC CARBON, ELEMENTAL CARBON, SULFATE,
22 NITRATE, AND ELEMENTS IN THE EMISSION RATES OF THIS 15
23 DIFFERENT TRUCKS.
24 WELL, IF YOU LOOK AT THIS CASE HERE, THIS IS
25 MILLIGRAM PER MILE. THE EMISSION GOES UP TO 5,400,

0041

01 5.4 GRAMS PER MILE BASICALLY FOR THE HIGHEST -- THIS IS
02 VEHICLE WHICH HAS THE 75 PERCENT OPACITY.

03 WHAT IS INTERESTING TO -- TO NOTE IS IT'S
04 VERY HIGH PERCENTAGE OF ELEMENTAL CARBON, AND THIS IS
05 BASICALLY FOR ALL OF THEM.

06 SO THE AVERAGE, IT WAS LIKE 75 PERCENT OF
07 ELEMENTAL CARBON, AND MUCH LOWER THAN 20 PERCENT AN
08 AVERAGE OF ORGANIC CARBON, NOT VERY MUCH OF ION, ONLY A
09 LITTLE OF ELEMENTS HERE IN THIS -- THIS TWO.

10 THERE WERE SOME REPLICATES, SIX, SEVEN, IS
11 THE REPLICATE, DONE WITH DIFFERENT CYCLE. AND THEN 14, 15
12 IS REPLICATE, AND 12, 13, THOSE ARE THE SAME VEHICLES
13 TESTED WITH DIFFERENT CYCLE. AND THEY ARE KIND OF
14 SIMILAR, AT LEAST IF YOU WOULD LOOK HERE.

15 CENTRAL DIESEL DISTRICT, IT SAYS A LITTLE BIT
16 MORE, IT TENDS TO PRODUCE MORE BECAUSE IT IS SUPPOSED TO
17 REPRESENT URBAN DRIVING.

18 WELL, I MENTIONED THAT THIS -- THAT WE ARE
19 DOING A LOT OF ORGANICS HERE FOR OUR PROFILING, AND THIS
20 IS BASICALLY THE LIST OF COMPOUNDS WHICH WE USE FOR
21 ORGANIC PROFILING. I'M NOT REALLY GOING TO TALK MORE
22 ABOUT IT. THOSE ARE ALL POLYCYCLIC AROMATIC HYDROCARBONS,
23 AND THEY ARE LISTED HERE IN THE ORDER OF POLLUTION FROM
24 THE CHROMATOGRAPHIC COLUMN FROM THE LATEST, NAPHTHALENE
25 UP, TO VERY HEAVY, CORONENE.

0042

01 THOSE WERE WHAT IS ONLY WHAT I WOULD LIKE TO
02 SHOW IS IN THIS FIRST COLUMN, THEY ARE MOSTLY GAS PHASE
03 P.A.H.'S, BECAUSE THOSE ARE LIGHT P.A.H.'S. THOSE ARE
04 CONTAINED IN THE GAS PHASE.

05 THIS COLUMN HERE CONTAINS MOSTLY P.A.H.'S
06 WHICH ARE DISTRIBUTED BETWEEN GAS PHASE AND PARTICLE
07 PHASE.

08 AND THEN FINAL COLUMN HERE, IT'S MOSTLY
09 PARTICLE PHASE P.A.H.'S. SO WE ARE DOING BASICALLY BOTH
10 PHASES. WE ARE DOING -- WE'RE COLLECTING COMPOUNDS WHICH
11 ARE BOTH IN THE GAS PHASE, AND IN THE PARTICLE PHASE, EVEN
12 IF WE ARE TALKING ABOUT THE PORTION OF THE PARTICLES.

13 HOWEVER, SINCE THIS DISTRIBUTION IS VERY MUCH
14 DEPENDENT ON TEMPERATURE AND SOME OTHER FACTORS, WE
15 BELIEVE IT'S IMPORTANT ESPECIALLY FOR THE COMPOUNDS WHICH
16 ARE DISTRIBUTED BETWEEN PHASES TO COLLECT THEM ALL.
17 BECAUSE THEN YOU HAVE THE SAME THING BETWEEN SOURCE AND
18 THE RECEPTOR. SO WE LOOK IN THE SAMPLE.

19 WELL, HOW ORGANICS LOOKS LIKE? THIS IS THE
20 SAME 15 SAMPLES FROM HEAVY-DUTY DIESEL, AND THOSE ARE ALL
21 COMPOUNDS, AT LEAST IN THE GROUP OF COMPOUNDS. I CANNOT
22 SHOW ALL 68, BUT I GROUP THEM TOGETHER, AND FROM
23 METHYLNAPHTHALENE TO CORONENE IN DIFFERENT VEHICLE.

24 IF YOU LOOK AT THIS LAST VEHICLE HERE, WHICH
25 IS REALLY VERY HEAVY IN METERS, IT DOESN'T EMIT A LOT OF

0043

01 ORGANICS, BUT IT DOES EMIT A LOT OF ELEMENTAL CARBON, FOR
02 EXAMPLE. SO IT DOESN'T NECESSARILY MEAN IF IT EMITS A LOT
03 OF CARBON, IT DOESN'T NECESSARILY EMIT A LOT OF P.A.H.'S.
04 THERE COULD BE SOME OTHER ORGANICS, TOO.

05 WELL, THIS CONTAINS A LOT OF GAS PHASE, AND
06 WHAT YOU CAN SEE HERE, THE GAS PHASE P.A.H.'S, THE FIRST
07 FOUR P.A.H.'S, ARE REALLY THE MOST ABUNDANT. SO IT WAS
08 INTERESTING TO LOOK ALSO IN THE PARTICLE P.A.H.'S, HOW
09 THEY LOOK LIKE.

10 AND FOR -- YOU CAN SEE THE SAME THING THAT IT
11 IS NOT NECESSARILY THE HIGHEST VEHICLE WITH THE HIGHEST
12 P.A.H.'S IN THERE, BUT THEY ALL LOOK KIND OF VERY -- VERY
13 SIMILAR. SO AT LEAST IN THIS GROUP OF 15 VEHICLE, WE HAD
14 A DEFINITE PATTERN OF THE P.A.H.'S, HOW THEY ARE
15 EMITTING.

16 ALSO, WHAT IS INTERESTING TO NOTE IS THAT
17 THIS MIDDLE P.A.H.'S HERE ARE MUCH MORE ABUNDANT THAN THE
18 HEAVY P.A.H.'S AT THE END, AND LIKE, FOR EXAMPLE, CORONENE
19 IS VIRTUALLY NOT PRESENT IN THIS EMISSION. IT IS PRESENT
20 IN VERY LOW AMOUNTS.

21 SO IT WAS INTERESTING FOR ME TO LOOK -- OH,
22 JUST TO -- LIKE TO MENTION, TOO, THAT WE WERE LOOKING AT
23 NOT ONLY P.A.H.'S, BUT IN HOPPING AND STERINGS (PHONETIC)
24 WHICH ARE TRACERS FOR ALL LUB (PHONETIC) BASICALLY BECAUSE
25 THEY ARE COMING FROM UNBURNED LUBRICATED OIL, AND THOSE

0044

01 COMPOUNDS ARE ALSO EMITTED IN VERY LOW AMOUNTS. THEY
02 TURN OUT NOT TO BE SO IMPORTANT. SO I WILL CONCENTRATE
03 MOSTLY ON P.A.H.'S.

04 SO I WOULD LIKE TO COMPARE THIS DATA WITH
05 THE -- OUR NEVADA DATA WHEN WE WERE TESTING MOSTLY
06 LIGHT-DUTY GASOLINE VEHICLE. IT'S A VERY BUSY TABLE. I
07 REALIZE THAT. IT'S JUST ONLY TO SHOW YOU THAT WE WERE
08 TESTING 24 VEHICLE, LIGHT-DUTY GASOLINE, IN THE RANGE FROM
09 LIKE '76 TO 1990, AND THEY WERE FEW VISIBLE SMOKE
10 EMITTERS. SO THEY WERE EMITTING VISIBLE SMOKE BASICALLY.
11 THERE WERE SIX OF THEM.

12 THE OTHER WERE NOT NECESSARILY DIESEL SMOKE,
13 BUT THEY HAD SOME HIGH P.M. EMISSIONS AS WELL, AND THEY
14 WOULD KIND OF DISTRIBUTE IT BETWEEN DIFFERENT AGES.

15 THIS -- THIS SLIDE SHOW MAYBE BETTER WHAT IS
16 THE DISTRIBUTION OF THE EMISSION RATES. SO P.M. EMISSION
17 RATES WERE VERY HIGH, FOR ESPECIALLY FOR THIS GROUP. IT
18 IS LIKE 1400 MILLIGRAM PER MILE. IT'S BASICALLY IN THE
19 DIESEL RANGE.

20 AND FOR SOME OF -- THEY WERE REALLY VERY LOW.
21 SO WE CAN TALK HERE ABOUT HIGH EMITTERS AND LOW EMITTERS,
22 SMOKERS AND NO SMOKERS.

23 THIS IS VERY SIMILAR SLIDE. I WILL SHOW IT
24 FOR HEAVY-DUTY DIESEL. THIS SHOWS THE ORGANIC CARBON AND
25 ELEMENTAL CARBON AND SOME IONS HERE FOR NONSMOKING

0045

01 VEHICLE, BUT EVEN NONSMOKING, THEY WERE SOME WHICH WERE
02 EMITTING UP TO 250 MILLIGRAMS PER MILE, BUT WE CAN SEE
03 THERE IS A LIGHT DISTRIBUTION BETWEEN THEM.

04 WHAT IS INTERESTING TO LOOK AT THE HIGH --
05 MUCH HIGHER PERCENTAGE OF ORGANIC CARBON THAN IN DIESEL.
06 IT WAS APPROXIMATELY 75 PERCENT FOR MINI-VALUE FOR THIS --
07 THIS CARS.

08 THERE IS NO MANY ITEMS, ONLY ONE, SOME
09 SULFATE, AND IT WAS KIND OF A LITTLE BIT STRANGE.

10 FOR A SMOKING VEHICLE -- WE CALLED IT SMOKING
11 VEHICLE SINCE THEY EMIT VISIBLE SMOKE. I KNOW IT'S NOT
12 VERY GOOD TERM, BUT IT'S EASIER TO SAY THIS WAY. AND
13 THOSE ARE -- THESE ARE DISTRIBUTION BETWEEN DIFFERENT --
14 THEY HAVE VERY DIFFERENT EMISSION RATES AS WELL, SOME
15 WHICH ARE QUITE LOW, EVEN IF THEY EMIT VISIBLE SMOKE, AND
16 SOME ARE VERY, VERY HIGH.
17 AND WHAT IS INTERESTING THAT ORGANIC CARBON
18 IS VERY HIGH. IT'S IN THE RANGE OF 90 PERCENT FOR THIS
19 VEHICLES.
20 WE LOOK AT THE P.A.H. EMISSIONS AS WELL, AND
21 THIS IS THE -- THIS IS THE MILLIGRAM PER MILES, AND I
22 JUST -- WHAT I DID, I JUST COMBINED SMOKERS AND NONSMOKERS
23 AND LOW P.M. EMITTING VEHICLE AND HIGH P.M. EMITTING
24 VEHICLE. LOW P.M. IT'S THE AVERAGE FOR VEHICLE WHICH IS
25 BELOW 50 MILLIGRAMS PER MILE, AND HIGH IS AVERAGE FOR MORE
0046 THAN 150 MILLIGRAMS PER MILE.
02 SO YOU CAN SEE THAT THE GAS PHASE P.A.H.'S
03 ARE EMITTED QUITE -- IN QUITE BIG AMOUNTS, BUT YOU CAN SEE
04 THOSE ARE THE HIGHEST MOLECULAR WEIGHT P.A.H.'S. AND I
05 WOULD LIKE TO SHOW IT FOR PARTICULATE P.A.H.'S, WHAT IS
06 INTERESTING IS TO LOOK AT THE CORONENE, FOR EXAMPLE, WHICH
07 IS REALLY EMITTED IN QUITE BIG AMOUNTS FOR HIGH P.M. AND
08 NONSMOKERS.
09 THERE IS, HOWEVER, ONE IMPORTANT THINGS THAT
10 I HAVE TO TELL, THAT THIS EMISSION RATES ARE NOT VERY
11 USEFUL PROFILES BECAUSE THEY COULD BE VERY BIG DIFFERENCES
12 IN EMISSION RATES, BUT IF THE COMPOUNDS ARE EMITTED IN THE
13 SAME PROPORTION, THE PROFILE WILL BE COLLINEAR.
14 WHAT WE DO FOR PROFILES WE USE WEIGHT
15 FRACTION, OR WEIGHT PERCENT. SO WE DIVIDE THE
16 CONCENTRATION OF GIVEN COMPOUNDS BY USUALLY SOME OF
17 SPECIES WE MEASURE, OR RATHER BY MASS.
18 SO EITHER OF THESE, IT IS EITHER A
19 CONSTRUCTIVE SPECIES OR MASS, GRAVIMETRIC MASS COLLECTED
20 ON THE -- ON THE FILTER.
21 SO IF I DO THAT FOR THIS TYPE OF A -- THEN WE
22 HAD A DIFFERENT -- DIFFERENT -- IT LOOKS A LITTLE BIT
23 DIFFERENT. NONSMOKERS REALLY EMIT ON THE WEIGHT PERCENT
24 MUCH MORE THAN SMOKERS OF P.A.H.'S. THIS IS BASED ON
25 THEIR WEIGHT PERCENT, OF COURSE, AND THIS WOULD HELP US TO
0047 DISTINGUISH BETWEEN THE DIFFERENT GROUPS OF -- OF
02 COMPOUNDS -- OF VEHICLE.
03 AND THIS LOOKS VERY SIMILAR FOR -- FOR HEAVY
04 P.A.H.'S, AND AGAIN, CORONENE IT'S VERY IMPORTANT HERE.
05 WELL, I REALIZE THAT THIS IS A LITTLE BIT
06 LONG SO I'M -- I HAVE TO SKIP SEVERAL SLIDES I HAVE HERE,
07 AND TALK A LITTLE BIT OUR DATA FROM INSPECTION AND
08 MAINTENANCE FROM PHOENIX, ARIZONA. AND THIS IS JUST HOW
09 MANY DIFFERENT TRUCKS WERE -- WERE TESTED OVER THERE.
10 THEY WERE DIFFERENT -- SEVEN RUNS AND EVERY
11 RUN HAS AROUND 15 TO -- 12, 15, 17 TRUCKS, IN THAT
12 ALTOGETHER IT WAS 99 TRUCKS AND DISTRIBUTED BETWEEN THE
13 DIFFERENT RUNS.
14 WHAT IS IMPORTANT TO NOTICE THAT ALL

15 BASICALLY WERE A VERY LOW OPACITY BECAUSE THE TRUCKS WERE
16 GOING TO BE INSPECTED AND THE CUTOFF POINT IS 20 PERCENT.
17 SO THEY ALL WERE QUITE LOW EMITTING -- EMITTING TRUCKS.
18 WE DON'T HAVE, OF COURSE, THE EMISSION RATES
19 FOR THIS TYPE OF TEST, BUT WE HAVE PROFILES. SO THIS IS
20 P.A.H. PROFILE FROM -- FOR THIS TRUCKS, AND IT LOOKS
21 REALLY QUITE SIMILAR AS FAR AS P.A.H.'S ARE CONCERNED TO
22 TRUCKS WHICH WERE -- WHICH WERE TESTED IN N.F.R.A.Q.S.
23 SO EVEN IF IT -- WE SAW SUCH A DIFFERENCE IN
24 THE EMISSION COMPOSITION ELEMENTAL AND INORGANIC CARBON,
25 THE P.A.H. ARE SIMILAR. THIS IS IN WEIGHT PERCENT. AND
0048
01 THIS IS ESPECIALLY VISIBLE WHEN WE LOOK AT HIGHER P.A.H.
02 AGAIN, QUITE A LOT OF P.A.H.'S IN THE AREA, IN THE MIDDLE
03 AREA, NOT VERY MANY IN THE VERY HIGH AREA.
04 I WOULD LIKE TO SHOW YOU JUST MAYBE ONE OR
05 TWO SLIDES FROM LIGHT-DUTY GASOLINE TESTING FROM
06 INSPECTION AND MAINTENANCE, AND AGAIN, WE WERE DOING SIX
07 RUNS OF APPROXIMATELY 120 VEHICLES TESTED. SO IT IS A BIG
08 POPULATION OF VEHICLE.
09 THE PROBLEM WE HAD, HOWEVER, THAT IN EVERY
10 RUN THERE WERE SOME OLD CARS, AND SOME WHICH WERE EMITTING
11 MORE THAN OTHER. IT MEANS THAT THE PROFILE ARE GOING TO
12 BE INFLUENCED BY HEAVY EMITTING VEHICLE, AND WE DON'T KNOW
13 IF THEY WERE PARTICLE -- HEAVY PARTICLE EMITTING VEHICLE
14 OR NOT SINCE INSPECTION MAINTENANCE DOESN'T MEASURE THIS.
15 BUT IF WE LOOK AT THE PROFILES OF DIFFERENT
16 RUNS, WE CAN SEE THAT THEY ARE VERY SIMILAR BASICALLY TO
17 THOSE WHICH WE HAD FROM NEVADA FOR HIGHER EMITTING
18 VEHICLE, AND QUITE A LOT OF GAS PHASE P.A.H.'S, BUT ALSO
19 VERY IMPORTANT HIGHER MOLECULAR WEIGHT P.A.H.'S HERE.
20 AND SIMILAR FOR THE HIGHER MOLECULAR WEIGHT,
21 YOU CAN SEE CLEARLY CORONENE HERE AND SOME HIGHER
22 MOLECULAR WEIGHT HERE, WHICH WERE NOT REALLY VISIBLE IN
23 DIESEL.
24 WHEN WE PUT THIS TOGETHER, I JUST WOULD LIKE
25 TO SHOW YOU SOME PROFILES WHICH ARE LIKE SUMMARIZED
0049
01 TOGETHER FOR ALL DIESEL TRUCKS FROM N.F.R.A.Q.S. STUDY.
02 YOU CAN SEE THIS IS ORGANIC CARBON, ELEMENTAL
03 CARBON, THEN WE HAVE SOME HOPPING TO A VERY NOT VISIBLE IN
04 THE PROFILE, AND WE HAVE P.A.H.'S GAS PHASE AND PARTICLE
05 PHASE. YOU CAN SEE THE P.A.H. GAS PHASE ARE VERY, VERY
06 LITTLE. THEY ARE REALLY NOT VERY IMPORTANT HERE, AND
07 THE -- THE VERY SIMILAR THINGS WE CAN SEE FROM INSPECTION
08 AND MAINTENANCE. GAS PHASE P.A.H.'S ARE REALLY VERY TINY
09 FRACTION OF THE WHOLE EMISSION, EVEN IF ORGANIC CARBON WAS
10 MUCH HIGHER HERE.
11 AND IN CONTRAST, FOR LIGHT-DUTY GASOLINE
12 VEHICLE FOR PHOENIX, WE CAN SEE THESE GAS PHASE P.A.H.'S,
13 THOSE ARE THIS RED HERE, ARE VERY HIGH. IT IS ABOVE 1,
14 BECAUSE IT IS EVERYTHING GAS PHASE. SO ANYTHING WHICH IS
15 ABOVE 1 IS A GAS PHASE.
16 AND THIS IS BASICALLY SOMETHING WHICH HELPS
17 US TO DISTINGUISH BETWEEN DIFFERENT CLASS COMPOUNDS OF THE
18 VEHICLE.
19 SO JUST TO FINISH THIS VERY BRIEF

20 PRESENTATION, I REALIZE A LOT OF DATA WHICH I JUST CAN
21 ONLY SUMMARIZE HERE, I HAVE TO SAY FIRST OF ALL THAT EVEN
22 IF LIGHT-DUTY GASOLINE VEHICLES DO EMIT PARTICULATE METAL,
23 THAN MOST OF THE EMISSION COMING FROM THE OLDER,
24 POOR-MAINTAINED VEHICLE.
25 THE MIXED PHASE PROFILES WHICH I WAS TALKING
0050
01 ABOUT GAS AND PARTICLE PHASE SPECIES CAN BE REALLY
02 UTILIZED TO APPORTION FINAL PARTICULATE METAL EMITTED FROM
03 GASOLINE- AND DIESEL-POWERED VEHICLES. SO WE CAN
04 DISTINGUISH BETWEEN THESE TWO, BASED ON THAT.
05 AS WELL AS USING EXTENDED PROFILES WHICH IS
06 INORGANIC AND ORGANIC SPECIES IN THE C.M.B. APPORTIONMENT
07 OF FINAL PARTICULATE METAL. IT REALLY ALLOWS US TO
08 DISTINGUISH BETWEEN DIFFERENT EVEN VEHICLE CATEGORIES. WE
09 DID IT FOR N.F.R.A.Q.S., AND WE CAN DISTINGUISH FOR
10 EXAMPLE BETWEEN SMOKING VEHICLE, BETWEEN COLD START,
11 BETWEEN HIGH EMITTING VEHICLE, AND BETWEEN DIESEL.
12 AND TO AGAIN, AS I POINTED OUT, MOST OF THE
13 DISCRIMINATORY POWER OF THE MIXED PHASE EXTENDED PROFILES
14 RESIDES IN THE POLYCYCLIC AROMATIC HYDROCARBONS. I'M NOT
15 TELLING YOU THAT THERE ARE OTHER COMPOUNDS AVAILABLE WHICH
16 COULD BE USED, BUT THOSE ARE CERTAINLY VERY GOOD
17 CANDIDATES WHICH MIGHT BE USED FOR PROFILING.
18 SO THIS IS BASICALLY ALL WHAT I HAD. JUST TO
19 SHOW YOU THAT THERE IS A POSSIBILITY OF BY DOING
20 CHEMICAL -- BY DOING CHEMICAL MASS BALANCE AND AMBIENT
21 MEASUREMENTS, THE POSSIBILITY OF KNOWING HOW MUCH
22 PARTICLES HAVE COMING FROM WHICH KIND OF VEHICLE.
23 AND AT THE END I WOULD JUST LIKE TO
24 ACKNOWLEDGE THE FINANCIAL SUPPORT OF NORTHERN FRONT RANGE
25 AIR QUALITY STUDY, AND E.P.A., AND TO GENERAL MOTORS AS
0051
01 WELL FOR NEVADA STUDY. THANK YOU.
02 DR. FROINES: NOW, I WANTED TO, AS I SAID, I FIRST
03 WANTED TO GIVE AN OPPORTUNITY TO JOE AND BARBARA TO
04 COMMENT ABOUT EACH OTHERS TALKS IF THEY CHOSE TO. IF NOT,
05 WE'LL JUST OPEN IT UP TO THE PANEL AND OTHER SPEAKERS.
06 DR. MAUDERLY: WHILE BARBARA IS GETTING DEFROCKED
07 THERE, WHY, I'LL JUST SAVE TIME BY STARTING AND ASKING
08 QUESTIONS AND VERY, VERY GOOD PRESENTATION. CERTAINLY YOU
09 SAID NOTHING I COULD ARGUE WITH, BUT I DO HAVE A QUESTION
10 AND THAT IS, I'M TRYING TO FORMULATE IN MY OWN MIND, IF I
11 WANT TO ASSUME AN ORGANIC FRACTION FROM EXHAUST PARTICLES
12 IN CITY ATMOSPHERES, WHAT IS A GOOD SORT OF AVERAGE RULE
13 OF THUMB ORGANIC FRACTION TO ASSUME?
14 I MEAN, FOR INSTANCE, YOU MENTIONED ONCE THAT
15 MOST OF THEM WERE BELOW 20 PERCENT. SOME DATA ARE HIGHER,
16 SOME ARE LOWER. I KNOW WITH OUR OWN STUDY, WE WENT FROM
17 AN OLD ENGINE THAT HAD 20 PERCENT, AND THE NEXT STUDY, IT
18 WAS ONLY 8 PERCENT. I MEAN, THAT BECOMES IMPORTANT IN
19 SOME CALCULATIONS OF DOSE.
20 WHAT -- WHAT WOULD BE A GOOD CONTEMPORARY
21 FIGURE TO USE?
22 DR. ZIELINSKA: THERE IS A PROBLEM BECAUSE IT'S --
23 LIKE I WAS SHOWING YOU, IT REALLY DEPENDS ON THE AREA AND
24 WHAT -- HOW THE VEHICLE REALLY LOOKS LIKE. BUT I THINK

25 PERSONALLY, IF YOU TAKE SOME KIND OF MEAN VALUE,
0052
01 70 PERCENT IS TOO HIGH, LIKE 30 OR 40 PERCENT FOR
02 ELEMENTAL ORGANIC -- OR ELEMENTAL, LET'S SAY, I'M TALKING.
03 OKAY. FOR ELEMENTAL TO BE 30, 40 THAT WOULD BE TOO LOW.
04 BUT I THINK IF YOU GO AROUND 50, RIGHT NOW,
05 FOR THE NEWEST VEHICLE. IT PROBABLY WOULD BE VERY -- VERY
06 REALISTIC BECAUSE WE HAVE ALL OF THIS MIXTURE ON THE ROAD
07 OF DIFFERENT VEHICLE -- DIFFERENT -- DIFFERENT, YOU KNOW,
08 AGE AND DIFFERENT -- DIFFERENT TECHNOLOGY, DIFFERENT
09 EMISSION.
10 SO THIS WOULD KIND OF BE THE RULE OF THUMB,
11 BUT I STILL NOT COMPLETELY SURE. I THINK WE NEED A LITTLE
12 MORE COMPARISON AND DOING A LITTLE BIT MORE BIGGER VEHICLE
13 POPULATIONS BECAUSE, YOU KNOW, ALL OF THIS -- OF THIS
14 DYNAMOMETER STUDY IS HOW MUCH? 15 MAYBE THE MOST VEHICLE?
15 AND WE ARE SUPPOSED REPRESENT EVERYTHING.
16 DR. MAUDERLY: DID I UNDERSTAND YOU CORRECTLY NOW
17 THAT YOU ARE SAYING YOU THINK 50 PERCENT --
18 DR. ZIELINSKA: I THINK IT WOULD BE --
19 DR. MAUDERLY: -- ORGANIC, SOLUBLE ORGANIC?
20 DR. ZIELINSKA: NO. FOR ELEMENTAL.
21 DR. MAUDERLY: OKAY. I'M ASKING FOR A --
22 DR. ZIELINSKA: FOR ORGANIC?
23 DR. MAUDERLY: -- AN AVERAGE ORGANIC FRACTION.
24 DR. FROINES: ARE YOU ASKING DIESEL OR GASOLINE OR
25 BOTH?
0053
01 DR. ZIELINSKA: DIESEL, I HOPE.
02 DR. MAUDERLY: WELL, DIESEL, SHE SHOWED DATA FOR
03 BOTH, I THINK. AND OF COURSE, ONE INTERESTED IN BOTH IF
04 THEY ARE INTERESTED IN THE TOTAL POOL OF MATERIAL THAT IS
05 OUT THERE, BUT DIESEL WOULD BE FINE.
06 DR. ZIELINSKA: YEAH, I WOULD THINK --
07 DR. MAUDERLY: I MEAN IS 20 PERCENT A REASONABLE
08 NUMBER?
09 DR. ZIELINSKA: NO, I THINK IT IS A LITTLE TOO LOW
10 FOR 20 PERCENT.
11 DR. MAUDERLY: LOW.
12 DR. ZIELINSKA: IT'S LOW FOR ORGANIC. I THINK IT
13 IN THE ORDER OF 30, 40 PERCENT REALLY.
14 DR. MAUDERLY: FOR DIESEL?
15 DR. ZIELINSKA: FOR DIESEL. BUT IT'S AGAIN, IT'S
16 A -- YOU KNOW, IT'S A VERY MEAN VALUE. IT COULD BE ENOUGH
17 STUDY AND AVERAGE THIS, IT MIGHT BE A LITTLE BIT DIFFERENT.
18 DR. MAUDERLY: THANK YOU.
19 DR. FROINES: AND SEE, IT'S NOT FAIR TO BE THE
20 CHAIR AND THEN TO PICK IN ON THE TWO OF YOU TALKING, BUT
21 I'LL DO IT ANYWAY.
22 IF IT'S 30 TO 40 PERCENT, WHAT PERCENT OF
23 THAT DO YOU THINK IS IN THE VAPOR PHASE?
24 DR. ZIELINSKA: OH, I'M NOT TALKING ABOUT VAPOR
25 PHASE HERE AT ALL. THE PERCENTAGE OF VAPOR PHASE MIGHT BE
0054
01 MUCH HIGHER THAN THAT. I'M TALKING ABOUT WHAT IS
02 ASSOCIATED WITH PARTICLES.
03 HOWEVER, DIESEL IN GENERAL DON'T EMIT VERY

04 MUCH -- VERY GAS PHASE, SO WE CAN -- YOU CAN SEE IT FROM
05 THERE, EVEN THOSE P.A.H.'S WHICH IS KIND OF
06 REPRESENTATIVE. SO THE GAS PHASE IS REALLY NOT VERY BIG
07 PERCENTAGE.

08 DR. FROINES: THE GAS PHASE IS INTERESTING IN
09 LOS ANGELES, OF COURSE, WHERE YOU GET A LOT OF NITRATION
10 ASSOCIATED WITH OUR --

11 DR. ZIELINSKA: YES.

12 DR. FROINES: -- OUR AMBIENT AIR AND THAT PARTICLES
13 THAT -- I MEAN RATHER VOLATILES WILL BECOME NITRATED AND
14 MAY END UP BEING PARTICLE ASSOCIATED --

15 DR. ZIELINSKA: YES.

16 DR. FROINES: -- SO YOU HAVE A DIFFERENT CHEMISTRY
17 GOING ON.

18 DR. ZIELINSKA: YES. IT'S TRUE. IT'S QUITE A LOT
19 FLUORANTHENE AND PYRENE, FOR EXAMPLE, THAT IS PART OF THIS
20 WHICH IN THE GAS PHASE, AND THIS COULD REACT WITH O.H.I.
21 FOLLOWED BY AND NATURAL REACTION FORMING NITROPYRENES OR
22 NITROFLUORENE.

23 DR. FROINES: IT SHOWS THAT THERE'S STILL CONTINUED
24 WORK NEEDED ON LOOKING AT P.A.H. COMPOSITION IN BOTH
25 GASOLINE AND DIESEL VEHICLES, IT SEEMS TO ME, BECAUSE

0055

01 IT'S -- AS WE GET INTO THE MORE HEALTH ORIENTED WE --
02 WE -- IF WE DON'T HAVE THAT DATA, IT'S VERY DIFFICULT TO
03 DEVELOP QUANTITATIVE ESTIMATES OF EXPOSURE AND THEN
04 SUBSEQUENTLY, SUBSEQUENT RISK.

05 DR. ZIELINSKA: WELL, OUR WORK WAS REALLY NOT FROM
06 THE POINT OF HEALTH EFFECT. IT WAS MOSTLY JUST TO OBTAIN
07 PROFILES TO GET A GOOD COMPOUNDS WHICH WOULD BE USED FOR
08 PROFILING. BUT AT THE SAME TIME, YOU HAVE A LOT OF DATA
09 AND P.A.H.'S AS WELL.

10 DR. FROINES: QUESTION. GARY FIRST. GARY AND THEN
11 PETER AND THEN JIM.

12 DR. FRIEDMAN: THIS IS A QUESTION FOR DR. MAUDERLY.
13 YOU SHOWED A SLIDE OF A RAT LUNG TUMOR THAT
14 LOOKED TO ME -- I'M NOT A PATHOLOGIST, BUT IT LOOKS SORT
15 OF LIKE A CYST CONTAINING CAROTENE MATERIAL.

16 WERE YOU SAYING THAT THAT IS TYPICAL OF THE
17 RAT LUNG TUMORS THAT ARE USED TO ESTIMATE RISK IN HUMANS,
18 OR IS THIS AN ATYPICAL ONE OR IS THAT WHAT THEY ALL LOOK
19 LIKE?

20 DR. MAUDERLY: WELL, THEY ARE NOT ATYPICAL, BUT NO,
21 THAT'S NOT THE TYPE OF LESION THAT'S BEING USED CURRENTLY
22 IN RISK ASSESSMENTS. THE REASON I SHOWED IT WAS AS -- AS
23 AN ILLUSTRATION, ANOTHER ILLUSTRATION OF THE MARKED
24 DIFFERENCES BETWEEN THE CELLULAR RESPONSES OF THE SPECIES.
25 THAT PARTICULAR LESION, WHICH WE DO NOT CALL

0056

01 A TUMOR, MOST PEOPLE IN THE UNITED STATES DON'T. THERE
02 ARE SOME PEOPLE WHO DO, ALTHOUGH THEY READILY ADMIT THAT
03 THAT KIND OF LESION DOES NOT OCCUR IN HUMANS, THAT -- THAT
04 TYPE OF LESION IS NOT TYPICAL OF OTHER SPECIES.

05 IT'S TYPICAL OF THE RAT. IT'S VERY
06 DISTINCTIVE. IN SOME STUDIES, IT'S IN HIGH PREVALENCE;
07 THAT IS, IT CONSTITUTES OR IT AFFECTS A NUMBER OF THE
08 ANIMALS.

09 NOW, FOR A NUMBER OF YEARS THERE WAS A DEBATE
10 AS TO WHETHER THAT LESION SHOULD BE COUNTED IN -- IN THE
11 TUMOR COUNT, IF YOU WILL, FROM WHICH RISK ASSESSMENTS WERE
12 DEVELOPED.

13 AT THIS TIME, IT IS NOT BEING COUNTED BECAUSE
14 IT'S -- IT'S ESSENTIALLY UNIVERSALLY AGREED THAT IT IS NOT
15 APPLICABLE.

16 SO THE REASON I SHOWED IT WAS NOT THAT IT WAS
17 THE PREDOMINANT LESION, AND I SHOWED YOU NO OTHER TUMOR
18 TYPES REALLY, BUT TO -- AS AN ILLUSTRATION THAT THERE ARE
19 MARKED DIFFERENCES IN THE CELLULAR RESPONSES.

20 DR. FRIEDMAN: WHAT DO THE TUMORS THAT ARE USED TO
21 ESTIMATE HUMAN RISK, WHAT DO THEY LOOK LIKE
22 HISTOLOGICALLY?

23 DR. MAUDERLY: WELL, I COULD SHOW THEM BUT DIDN'T
24 FOR TIME'S SAKE. THEY ARE ADENOMAS AND ADENOCARCINOMAS.
25 THERE ARE A FEW SQUAMOUS CELL CARCINOMAS, BUT THAT'S
0057

01 TYPICALLY A VERY SMALL PERCENTAGE.

02 A SUBSTANTIAL PORTION OF THE TOTAL TUMOR
03 COUNT, IF YOU WILL, ARE BENIGN TUMORS, ADENOMAS, AND THESE
04 RANGE IN SIZE FROM JUST VERY SMALL NODULES TO SUBSTANTIAL
05 LESIONS.

06 THE ADENOCARCINOMAS ARE VERY SIMILAR EXCEPT
07 IN THE CENTER OF THAT LESION, THEY PROGRESS, AND YOU'VE
08 LOST ANY SEMBLANCE OF NORMAL ARCHITECTURE AND SOMETIMES
09 THEY ARE NECROTIC IN THE CENTER.

10 SO THEY ARE ADENOMAS AND ADENOCARCINOMAS.
11 THEY ARE ALL PERIPHERAL TUMORS. THEY ARE NOT TUMORS OF
12 THE CENTRAL AIRWAYS IN THE RATS.

13 DR. FRIEDMAN: THANK YOU.

14 DR. FROINES: PETER.

15 DR. WITSCHI: YEAH. I WOULD LIKE TO COMMENT ON HOW
16 YOU SAW THE LAST SLIDE BECAUSE OF WITHIN THE CONSTRAINTS
17 WE HAVE IN ANIMAL NUMBERS, AND IF WE GO TO APPROPRIATE LOW
18 DOSES, WE WOULD GET EXACTLY THE SAME GRAPH FOR ANY
19 CARCINOGEN IN ANY TISSUE IN ANY SPECIES.

20 YOUR AST SLIDE REALLY DOES NOT ADDRESS AT ALL
21 THE QUESTION OF THRESHOLD OR NOT BECAUSE WE COULD GET THE
22 SAME ANSWER WITH ANYTHING.

23 DR. MAUDERLY: WELL, THAT'S EXACTLY WHY I SHOWED
24 THE SLIDE TO MAKE EXACTLY THE OPPOSITE POINT, AND THE
25 POINT IS THIS. THAT IS I -- I WAS PORTRAYING THAT THERE
0058

01 WAS A LARGE NUMBER OF GROUPS IN THAT LOW DOSE REGIME IN
02 WHICH THE DATA SHOWED NO SUGGESTION OF SLOPE. IT'S NOT
03 THE FACT THAT THEY WERE STATISTICALLY INSIGNIFICANT.
04 THAT'S NOT THE POINT. OF COURSE, THEY WOULDN'T BE AT THAT
05 LOW LEVEL.

06 BUT LET'S ASSUME THAT THERE WERE 200,000
07 ANIMALS PER GROUP, AND EACH ONE OF THOSE POINTS, THEY
08 STILL DO NOT CONSTITUTE A SLOPE. AND THERE WAS NO SLOPE
09 WITHIN THAT REGION.

10 NOW, IF THERE IS A RESPONSE IN THAT REGION,
11 THEN -- THEN ONE WOULD ASSUME THAT IN SO MANY STUDIES AND
12 SO MANY GROUPS THAT ONE WOULD BEGIN TO SEE A SLOPE, AND
13 YOU CAN PICK STUDIES IN WHICH THERE IS A POINT ABOVE THE

14 LINE. YOU CAN ALSO PICK STUDIES IN WHICH THERE IS A POINT
15 BELOW THE LINE.
16 BUT THE ABSENCE OF SLOPE IN THAT REGION,
17 COUPLED WITH THE FACT THAT THESE CELL RESPONSES DON'T
18 OCCUR UNTIL YOU GET UP IN THE HIGHER EXPOSURE REGIMES, I
19 THINK FITS TOGETHER, AND IT -- CONVINCINGLY TO ME THAT
20 THERE IS A THRESHOLD FOR THIS HIGH-DOSE-RESPONSE.
21 NOW, THAT DOES NOT MEAN THAT THERE IS NOTHING
22 OCCURRING IN THE RATS THAT HAS TO DO WITH THE ORGANIC
23 MUTAGENS. IT'S JUST THAT IF THERE IS, WE CERTAINLY HAVE
24 NOT BEEN ABLE TO SEE IT, EITHER FROM THE TUMOR RESPONSE OR
25 FROM THE D.N.A. ADDUCT WORK THAT'S BEEN DONE.

0059
01 DR. FROINES: JIM. I KNOW STAN'S GOING TO WANT TO
02 COMMENT ON THAT SO --
03 DR. GLANTZ: WELL, MY SHORT-TERM MEMORY IS -- I
04 THINK.
05 DR. SEIBER: WELL, MY QUESTION ISN'T ON THAT
06 SUBJECT. SO WHY DON'T YOU GO AHEAD AND FOLLOW UP.
07 DR. GLANTZ: WELL, I WAS ALSO BOTHERED BY THAT
08 SLIDE IN YOUR INTERPRETATION. COULD YOU MAYBE PUT IT UP
09 THERE JUST SO WE CAN ARGUE ABOUT IT WITH -- IN A REVERENT
10 WAY --
11 DR. MAUDERLY: I DON'T KNOW IF IT'S POSSIBLE FOR
12 THE PROJECTIONIST TO --
13 DR. GLANTZ: CAN YOU PUT THE SLIDE BACK UP?
14 DR. MAUDERLY: IT'S THE THIRD TO THE LAST.
15 DR. FROINES: JIM, DO YOU WANT TO TRY AND SNEAK IN
16 A QUESTION?
17 DR. GLANTZ: WELL, OKAY.
18 DR. MAUDERLY: ACTUALLY, I MAY HAVE THAT IN THE
19 VIEW GRAPH. I'M NOT SURE, BUT LET ME LOOK.
20 DR. GLANTZ: I MEAN, THE FIRST QUESTION I HAVE
21 WHICH I CAN ASK YOU WHILE YOU'RE LOOKING. IF YOU CAN LOOK
22 AT LISTEN AND THE SAME TIME. OH, THERE WE GO.
23 DR. MAUDERLY: YES.
24 DR. GLANTZ: NO, NOT THAT ONE. IT'S THE GRAPH IS
25 THE ONE WE WANT.

0060
01 DR. MAUDERLY: I'LL MOVE THIS UP HERE. THERE YOU
02 GO.
03 DR. GLANTZ: OKAY. WELL, THE FIRST QUESTION I HAD
04 IS WHAT IS THE DIFFERENCE BETWEEN THE OPEN CIRCLES AND THE
05 CLOSED CIRCLES?
06 DR. MAUDERLY: THE DIFFERENCE BETWEEN THE OPEN
07 CIRCLES AND THE CLOSED CIRCLES, AS I STATED, WAS THAT THE
08 CLOSED CIRCLES REPRESENT GROUPS IN WHICH THE STATISTICS
09 SHOWED A SIGNIFICANT DIFFERENCE FROM CONTROL.
10 THE OPEN CIRCLES DID NOT SHOW A SIGNIFICANT
11 DIFFERENCE. ALL OF THEM ARE TREATED GROUPS.
12 DR. GLANTZ: OKAY. WELL, I JUST MISSED THAT
13 DETAIL.
14 I MEAN, I THINK THOUGH IF YOU WERE -- IF YOU
15 TAKE ESPECIALLY THE LEVERAGE POINT THERE, THE ONE VERY
16 HIGH POINT OFF ON THE -- ON THE TOP POINT, RATHER, I MEAN,
17 IT JUST SEEMED TO ME THAT YOU COULD QUITE REASONABLY DRAW
18 A STRAIGHT LINE THROUGH THE REST OF THOSE POINTS THAT

19 WOULD END UP WITH AN INTERCEPT THAT WASN'T SIGNIFICANTLY
20 DIFFERENT FROM THE ORIGIN.
21 I MEAN, HAVE YOU TRIED THAT AND TESTED
22 WHETHER OR NOT YOU GET A SLOPE THAT'S -- THAT ENDS UP
23 PRETTY MUCH GOING THROUGH THE ORIGIN, OR WHETHER THERE IS
24 A STATISTICALLY DIFFERENCE IN THE INTERCEPT FROM ZERO?
25 DR. MAUDERLY: I HAVE NOT --

0061
01 DR. GLANTZ: WOULD --
02 DR. MAUDERLY: -- ALTHOUGH MANY PEOPLE HAVE
03 MASSAGED THESE DATA. I WOULD AGREE.
04 DR. GLANTZ: WELL, I'M NOT TALKING ABOUT
05 MASSAGING.
06 DR. MAUDERLY: NO, I THINK THAT IT IS CLEAR THAT
07 ONE COULD FIT A STRAIGHT LINE THROUGH THESE DATA, AS WE
08 OFTEN DO.
09 DR. GLANTZ: OKAY.
10 DR. MAUDERLY: I'M NOT ARGUING THAT.
11 DR. GLANTZ: WELL, BUT YOU SEE --
12 DR. MAUDERLY: I'M SAYING THAT ONE DOES NOT NEED TO
13 FIT LINES AND USE STATISTICS TO SEE THAT THERE IS NOTHING
14 HAPPENING IN THIS REGION.
15 DR. GLANTZ: WELL, EXCEPT I DON'T THINK THAT'S A
16 FAIR CONCLUSION TO DRAW FROM THESE DATA. I MEAN THAT'S
17 WHAT ONE DOES -- I MEAN, IT'S LIKE JOHN SAID, CHEMISTS
18 LOOK AS THESE FROM A CHEMICAL PERSPECTIVE, AND YOU KNOW, I
19 THINK -- I THINK THAT YOU'VE GOT SOME DATA THERE, AND I
20 MEAN, YOU COULD DO A FORMAL TEST TO SEE IF THERE'S A
21 THRESHOLD EFFECT, WHICH I WOULD BET YOU'RE GOING TO NOT BE
22 ABLE TO SHOW --
23 DR. MAUDERLY: STATISTICALLY --
24 DR. GLANTZ: STATISTICALLY --
25 DR. MAUDERLY: -- I WOULD BET WITH YOU --

0062
01 DR. GLANTZ: OKAY. WELL --
02 DR. MAUDERLY: -- THAT STATISTICALLY YOU CAN NOT
03 PROVE A THRESHOLD.
04 DR. GLANTZ: WELL, OKAY. AND FURTHERMORE, I MEAN,
05 IF -- IF YOU WERE TO HAVE JUST A SIMPLE STRAIGHT LINE
06 THERE, WHAT YOU WOULD EXPECT, AND THIS IS SORT OF THE
07 POINT THAT PETE MADE, THAT AS YOU GET DOWN CLOSE TO ZERO,
08 YOU ARE GOING TO START SHOWING SMALL EFFECTS, AND THE
09 THINK THE POINT YOU MADE ABOUT, YOU KNOW, WELL, YOU SEEM
10 TO SEE -- HAVE A FLAT EFFECT AT THE LOW DOSES, AND THEN
11 NOT A FLAT EFFECT.
12 I MEAN, THAT AGAIN, IS SOMETHING THAT YOU
13 COULD TEST. I MEAN, THERE ARE VERY STRAIGHT FORWARD,
14 SIMPLE STATISTICAL MEASURES THAT YOU COULD TEST FOR A TEST
15 THE COINCIDENCE BETWEEN THE REGRESSIONS IN THOSE TWO
16 POINTS EVEN.
17 AND I MEAN, I THINK THAT IT -- TO ME TO
18 JUST -- TO GET THE DATA AND TO PUT IT UP AND TO NOT GO
19 THROUGH THE FORMAL ANALYSIS OF IT IS -- IS REALLY A SHAME
20 BECAUSE THAT'S THE WHOLE REASON THAT ONE HAS STATISTICS,
21 IS TO TRY TO COME UP WITH SOME KIND OF QUANTITATIVE
22 ESTIMATE OF THE UNCERTAINTIES IN THE LACK OF PRECISION
23 THAT YOU RUN INTO IN MAKING THESE DECISIONS.

24 SO I MEAN, I THINK -- I MEAN, YOU'RE FREE TO
25 INTERPRET THESE -- OBVIOUSLY, FREE COUNTRY, BUT I MEAN,
0063
01 YOU'RE FREE TO INTERPRET THESE DATA HOWEVER YOU WANT, BUT
02 I MEAN, IF YOU WERE TO SHOW THIS TO ME, I WOULD COME UP
03 WITH -- WITH AN EQUALLY DEFENDABLE, I THINK,
04 INTERPRETATION THAT THERE ISN'T THE THRESHOLD, YOU KNOW.
05 AND I THINK, I MEAN, I'M VERY SURPRISED THAT
06 YOU DIDN'T SHOW US A FORMAL ANALYSIS TO EITHER SUPPORT OR
07 REFUTE THE ASSERTIONS THAT YOU'RE MAKING. BECAUSE IT'S A
08 PRETTY EASY THING TO DO WITH THE DATA YOU'VE GOT THERE.
09 DR. MAUDERLY: WELL, I'LL RESPECT THAT OPINION --
10 DR. GLANTZ: YEAH, AND I MEAN --
11 DR. MAUDERLY: -- AND I CAN'T ARGUE WITH THE FACT
12 THAT STATISTICALLY -- I'M AGREED. STATISTICALLY, I DON'T
13 THINK YOU CAN EVER PROVE A THRESHOLD. THE DATA ARE NOT
14 ROBUST ENOUGH DO THAT.
15 THE REASON THAT I SHOWED IT, AND I DO
16 CONSIDER THIS A STRONG SUPPORTING EVIDENCE FOR THE PREMISE
17 OF THE THRESHOLD, I'M COMING FROM THE OTHER SIDE. FROM
18 THE BIOLOGICAL SIDE, WE SEE A CLEAR THRESHOLD BETWEEN
19 THOSE EXPOSURE GROUPS IN WHICH THIS CHRONIC, INFLAMMATORY,
20 PROLIFERATIVE RESPONSE DOES NOT OCCUR, AND THOSE IN WHICH
21 IT DOES, AND THEN, OF COURSE, THERE'S THE GRAY ZONE.
22 NOW, MANY PEOPLE HAVE -- HAVE TREATED -- I'LL
23 NOT USE THE TERM MESSAGE. THAT'S PEJORATIVE.
24 MANY PEOPLE HAVE TREATED THESE DATA
25 STATISTICALLY. THEY'VE ALL BEEN IN THE LITERATURE FOR
0064
01 SOME TIME. CALIFORNIA AND OTHER PEOPLE HAVE HAD THE
02 OPPORTUNITY TO LOOK AT THEM, AND -- BUT WHAT'S TYPICALLY
03 BEEN DONE IS TO TAKE ONE STUDY AND START WITH ONE STUDY
04 WHERE YOU DON'T HAVE MANY GROUPS DOWN THERE. YOU MAY HAVE
05 ONE, AND TRY TO FIT LINES TO THAT.
06 AND -- AND THE CONCLUSION WOULD BE CLEAR.
07 YOU COULD REACH NO OTHER CONCLUSION STATISTICALLY THAN
08 THERE IS NO THRESHOLD.
09 BUT FROM A BIOLOGICAL RESPONSE STANDPOINT, WE
10 SEE A THRESHOLD, AND I THINK WHEN YOU LOOK AT THE TOTALITY
11 OF THE DATA IT -- WITHOUT FITTING LINES AND TESTING IT,
12 THE TOTALITY OF THE DATA DO -- ARE VERY CONSISTENT WITH
13 THAT BIOLOGICAL THRESHOLD.
14 SO IT IS TWO DIFFERENT WAYS OF LOOKING AT THE
15 SAME THING.
16 DR. FROINES: THE PROBLEM, STAN, OF COURSE, THAT
17 AGAIN, THE "N" VALUES HERE ARE SMALL. THIS ISN'T EXACTLY
18 THE MEGA MOUSE STUDY WITH 26,000 MICE. AND SO WE ARE --
19 THE STATISTICAL ANALYSIS IS GOING TO BE LIMITED BY THE
20 SIZE OF THE STUDY, AND SO YOU'RE -- IT'S GOING TO END UP
21 BEING AMBIGUOUS TO SOME LEVEL, I THINK.
22 DR. GLANTZ: CAN I JUST ASK ONE OTHER QUESTION,
23 PLEASE?
24 DR. FROINES: WE'RE VERY LATE ON TIME. WE HAVE A
25 LARGE NUMBER OF SPEAKERS.
0065
01 DR. GLANTZ: OKAY. WELL, I JUST HAVE ONE OTHER
02 QUICK QUESTION.

03 DR. FROINES: PEOPLE WANT ASK QUESTIONS.
 04 DR. GLANTZ: IF YOU COULD BACK UP TO THE OTHER --
 05 THE SLIDE WHERE YOU WERE COMPARING THE MICE AND THE
 06 RATS --
 07 DR. MAUDERLY: MICE AND THE RATS?
 08 DR. GLANTZ: -- WITH THE NUMBERS. SEE, I DON'T
 09 UNDERSTAND HISTOLOGY WITH NUMBERS OR --
 10 DR. MAUDERLY: OH, THAT'S WAY BACK.
 11 DR. GLANTZ: WAY BACK. I JUST HAD A QUICK QUESTION
 12 ABOUT THAT.
 13 DR. FROINES: STAN, BEFORE YOU ASK THE QUESTION. I
 14 SEE JIM WANTS TO ASK A QUESTION, GEORGE SAYS SOME STAFF
 15 HAVE QUESTIONS, WHICH WE MAY NOT GET TO. PAUL DOES, I DO,
 16 KATHIE DOES --
 17 DR. GLANTZ: OKAY. WELL, KEEP GOING.
 18 DR. FROINES: WE'RE IN -- WE'RE IN TIME TROUBLE
 19 HERE FOLKS --
 20 DR. GLANTZ: OKAY. WELL, GO BACK ONE MORE SLIDE.
 21 I'LL BE VERY FAST.
 22 DR. FROINES: -- SO WE'RE JUST GOING TO HAVE TO DO
 23 THE BEST WE CAN.
 24 DR. GLANTZ: NO. GO BACK ONE MORE. KEEP GOING
 25 BACK TO WHERE YOU WERE -- YEAH, THAT ONE.
 0066
 01 DR. MAUDERLY: OH.
 02 DR. GLANTZ: JUST REAL QUICKLY. I MEAN, YOU'VE GOT
 03 THE POINT ESTIMATE -- THIS IS ANOTHER STATISTICAL
 04 QUESTION.
 05 YOU'VE GOT THE POINT ESTIMATES. YOU DIDN'T
 06 SHOW US ANY MEASURES OF CERTAINTY ON THIS.
 07 DID YOU GUYS TEST TO SEE WHETHER THOSE
 08 DIFFERENCES ARE SIGNIFICANT?
 09 DR. MAUDERLY: YES. IN THE PUBLISHED PAPERS ON
 10 THIS, STATISTICS WERE DONE, ERROR BARS ARE GIVEN, ALL THAT
 11 IS DONE.
 12 THIS IS SIMPLY A SUMMARY SLIDE TO SHOW THAT
 13 THE TWO SPECIES RESPONDED DIFFERENTLY.
 14 DR. GLANTZ: OKAY. BUT WHEN YOU DID THAT, DID YOU
 15 SHOW -- ARE THESE -- I MEAN, IT'S QUITE BELIEVABLE, BUT
 16 THE -- THESE RATIOS YOU SHOW HERE ARE DIFFERENT FROM 1
 17 THEN, SIGNIFICANTLY DIFFERENT FROM 1?
 18 DR. MAUDERLY: YES, YES.
 19 DR. GLANTZ: OKAY. THANK YOU.
 20 DR. MAUDERLY: WELL, NOT ALL OF THEM. CLEARLY SOME
 21 OF THOSE ARE CLOSER TO 1. I MEAN, A 1.2 WOULDN'T BE
 22 SIGNIFICANT, BUT THE FACT THAT THE TWO SPECIES HAD QUITE
 23 DIFFERENT LEVELS OF INFLAMMATORY RESPONSE AND ANTI-OXIDANT
 24 DEFENSES, THAT'S CLEARLY SIGNIFICANT. AND YOU KNOW, I CAN
 25 REFER YOU TO THE PAPERS ON THAT.
 0067
 01 DR. GLANTZ: OKAY. THANK YOU.
 02 DR. FROINES: JIM, JIM SEIBER.
 03 DR. SEIBER: YES, THANK YOU.
 04 DR. MAUDERLY: MAYBE WE CAN HAVE THE SLIDES OFF ON
 05 THE PROJECTORS THERE SO WE DON'T --
 06 DR. SEIBER: I HAVE A QUESTION FOR EACH OF THESE
 07 PRESENTERS. CAN YOU HEAR ME OKAY?

08 YEAH, IT SEEMS A LITTLE WEAK, BUT I'LL GO
09 AHEAD, I'LL JUST SPEAK UP.
10 WITH REGARD TO EMISSIONS, DR. ZIELINSKA, I'M
11 CONCERNED OR INTERESTED IN EMISSION CHANGES OVER TIME.
12 BECAUSE IT SEEMS TO ME EMISSIONS ARE A FUNCTION OF A LOT
13 OF THINGS, THE TYPE OF VEHICLE, THE TYPE OF FUEL THAT YOU
14 USED, THE YEAR OF THE VEHICLE, AND OF COURSE, WEATHER
15 CONDITIONS, ET CETERA.
16 SOME OF THESE HAVE REALLY CHANGED THE
17 MATERIAL -- MATERIALLY OVER THE LAST FIVE, TEN YEARS, AND
18 WILL CONTINUE TO CHANGE. PARTICULARLY THE TYPE OF FUEL
19 AND THE EFFICIENCY OF THE ENGINE.
20 SO I WONDERED -- NOW -- NOW, MY CONCERN OR MY
21 INTEREST IS FRAMED BY A DRAFT STUDY THAT THE C.C.E.R.T.
22 GROUP HAS DONE AT THE UNIVERSITY OF CALIFORNIA, RIVERSIDE,
23 AND IT'S ONLY A DRAFT REPORT THAT WE WERE SHOWN, BUT THERE
24 WAS SOME RATHER SIGNIFICANT DIFFERENCES IN WHAT COMES OUT
25 OF THE TAILPIPE, HOW MUCH P.A.H. IS EMITTED, AND THE
0068
01 MUTAGENICITY ASSOCIATED WITH THOSE EMISSIONS.
02 CAN YOU -- CAN YOU COMMENT IN -- IN FAIRLY
03 SPECIFIC TERMS, AS WELL AS YOU CAN, ON THOSE CHANGES AND
04 HOW THAT MIGHT AFFECT WHAT -- WHAT PEOPLE ARE EXPOSED TO
05 OUT IN THE AMBIENT ENVIRONMENT?
06 DR. ZIELINSKA: CERTAINLY. THERE IS A LOT OF
07 CHANGES OCCURRING IN THE NEWER VEHICLE. BUT YOU HAVE TO
08 TAKE INTO ACCOUNT THAT WHAT WE ARE EXPOSED TO IS A MIXTURE
09 OF THINGS. VEHICLE ARE -- WE STILL HAVE HERE IN
10 CALIFORNIA VEHICLE FROM 20 YEARS OLD.
11 OKAY. SO IT'S -- WE CANNOT DISCARD THIS OLD
12 VEHICLE BECAUSE THEY -- BASICALLY, MOST OF THE EMISSION IS
13 COMING FROM THE OLDER VEHICLE, AS A MATTER OF FACT, AND
14 THIS IS THE SAME, NOT ONLY FOR GAS PHASE BUT FOR PARTICLE
15 AS WELL, ESPECIALLY FOR LIGHT-DUTY GASOLINE VEHICLE.
16 AND I WAS JUST TRYING TO SHOW THIS IN MY
17 PRESENTATION THAT MOST OF THAT 90 PERCENT OF EMISSION
18 PROBABLY COMES FROM LIKE 10 PERCENT OF THE VEHICLE FROM
19 P.M. -- AND SO THAT'S AN OLDER VEHICLE.
20 DR. SEIBER: WHAT ABOUT FUEL CHANGES THAT HAVE
21 OCCURRED IN THE LAST FIVE, TEN YEARS?
22 DR. ZIELINSKA: AS FAR AS OXYGENATED FUEL, IT
23 DOESN'T REALLY SEEMS TO AFFECT VERY MUCH THE PARTICLE
24 EMISSION FOR OLDER VEHICLE.
25 WE ARE GOING TO DO THE STUDY IN CONNECTION
0069
01 WITH N.F.R.A.Q.S. THIS YEAR, WHICH WE WILL BE TESTING
02 OXYGENATES IN THE FUEL; HOWEVER, OUR LAST YEAR DATA WERE
03 FROM DENVER WITH OXYGENATED FUEL. SO WE CAN -- WE CAN
04 KIND OF COMPARE THAT, AND WE DIDN'T SEE VERY MUCH
05 DIFFERENCE BETWEEN SUMMER AND THE -- AND THE WINTER.
06 WHAT IS IMPORTANT I THINK IS TO GROUP THIS
07 VEHICLE, LIKE WE DID IN DENVER, FOR EXAMPLE, STUDY, ON
08 OLDER VEHICLE -- EVEN NOT REALLY THE -- THE AGE, BUT HOW
09 THEY EMIT. LOW EMITTER, MEDIUM EMITTER, HIGH EMITTER,
10 COLD START, WARM START. WE HAVE PROFILES FOR EVERY ONE OF
11 THOSE, AND WE CAN COMPARE THAT.
12 DR. SEIBER: WHAT ABOUT THE DIESEL FUEL CHANGES

13 THAT HAVE OCCURRED?

14 DR. ZIELINSKA: I THINK SULFUR WAS THE MOST
15 IMPORTANT THING REALLY IN DIESEL FUEL CHANGE, AND WE DO
16 SEE THAT THERE'S NOT A LOT OF SULPHATES EMITTED ANYMORE ON
17 THE DIESEL. BEFORE IT WAS IN THE OLDER VEHICLE. YEAH, IT
18 WAS TRUE.

19 THE STUDY I WAS SHOWING FROM N.F.R.A.Q.S. ALL
20 RAN ON THE WINTER FUEL. SO THE FUEL HERE WAS VERY
21 CONSISTENT.

22 I -- I THINK THAT P.A.H.'S, AS FAR AS
23 EMISSION RATES, OF COURSE, IS VERY MUCH DEPENDENT ON THE
24 TYPE OF VEHICLE AND CONDITION, BUT WEIGHT FRACTIONS, IT'S
25 MORE CONSISTENT. WE CAN DO SOME GROUPING OF VEHICLE.

0070

01 HOWEVER, I'M NOT SO SURE EXACTLY HOW THE
02 GEOGRAPHICAL AREA DIFFERENCES IN FUEL CAN REALLY AFFECT
03 IT.

04 DR. SEIBER: WELL, LET'S SAY, IF YOU DID A TEST OF
05 VEHICLE EMISSIONS FROM TEN YEARS AGO AND DID ONE TODAY, ON
06 THE AVERAGE, WHAT WOULD YOU SEE IN TERMS OF P.A.H.
07 COMPOSITION IN PARTICULATE MATTER FROM DIESEL BURNING
08 ENGINES?

09 DR. ZIELINSKA: I THINK WE WOULD SEE MUCH LESS
10 EMISSIONS OF PARTICLES FROM NEWER TECHNOLOGY VEHICLES.

11 THERE IS A NEW CONCEPT, HOWEVER, COMING AND
12 THERE WAS SOME LATER STUDY PUBLISHED IN '96 THAT -- THAT
13 THE NEW ENGINE DESIGN ON THE -- ESPECIALLY ON THE
14 HEAVY-DUTY DIESEL, TENDS TO PUT MORE FINE PARTICLES --
15 ULTRAFINE PARTICLES, WHICH IS A CONCERN CURRENTLY
16 OCCURRING.

17 OKAY. YOU HAVE LESS MASS, BUT YOU HAVE MORE
18 PARTICLES, MUCH SMALLER PARTICLES AS A MATTER OF FACT.
19 BUT THIS IS SOMETHING WHICH COMING UP RIGHT NOW, AND
20 BASICALLY THERE'S NOT ENOUGH DATA YET CONCERNING THAT.

21 DR. SEIBER: THE SECOND QUESTION FOR DR. MAUDERLY,
22 GIVEN THAT THE PARTICLES CONSIST OF BOTH ELEMENTAL CARBONS
23 SOME INORGANICS AND SOME ORGANICS, IS IT POSSIBLE THAT THE
24 RESPONSE THAT YOU SEE IN RATS ARE DUE TO A COMBINATION OR
25 IS IT STRICTLY A PHYSICAL PARTICLE ASSOCIATED OR COULD --

0071

01 COULD THERE BE A ROLE FOR THE ASSOCIATED ORGANIC AND
02 INORGANIC FRACTION?

03 DR. MAUDERLY: WELL, I GUESS THE BEST ANSWER TO
04 THAT IS CERTAINLY THERE COULD BE. THAT IS, IF WE ARE
05 STARTING OUT AND WE DIDN'T HAVE DATA, AND -- AND WE WERE
06 HE SEEING A TUMOR RESPONSE AS WE DID WHEN WE WERE SEEING
07 THIS FIRST TEN YEARS AGO OR SO, IT -- IT'S VERY PLAUSIBLE
08 TO ASSUME THAT THE ORGANIC FRACTION, AND ITS MUTAGENIC
09 ACTIVITY, D.N.A. ADDUCTION AND ALL THESE SORTS OF THINGS
10 IS PLAYING A ROLE IN THE RESPONSE. OKAY.

11 THE DATA THAT WE HAVE THOUGH FROM STUDIES
12 THAT WERE DESIGNED TO TEST THAT HYPOTHESIS AS BEST WE
13 COULD SUGGESTS THAT IF THERE IS A ROLE OF THE ORGANIC
14 FRACTION IN THE RAT TUMOR RESPONSE, IT'S NOT EVIDENT.
15 IT'S NOT EVIDENT EITHER IN THE -- SLOPE OF THE INFAMOUS
16 CURVE WE WERE LOOKING AT OR IN THE TUMOR COUNTS WHEN YOU
17 COMPARE CARBONACEOUS MATERIAL TOTAL MASS AGAINST TOTAL

18 DIESEL SOOT, THE RESPONSE IS JUST AS LARGE WITH CARBON
19 BLACK OR WITH TITANIUM DIOXIDE, SOMETHING LIKE THAT.
20 NOW, IF WE ASK IT ANOTHER WAY AND SAY, WELL,
21 THAT TOTAL SOOT MASS THAT YOU'RE COMPARING ON CONSISTS OF
22 BOTH ORGANIC AND INORGANIC, SO DOES THE ORGANIC, TO THE
23 EXTENT THAT IT'S NOT RELEASED FROM THE PARTICLES, AND
24 THAT'S ANOTHER THING WE DON'T UNDERSTAND WELL IS THE
25 EXTENT TO WHICH IT'S BIOAVAILABLE IF YOU WILL, DOES --
0072
01 DOES IT PLAY A ROLE JUST BY CONSTITUTING SOME PORTION OF
02 THAT TOTAL MASS, THAT FOREIGN OBJECT IN THE LUNG. AND I
03 WOULD ASSUME THAT IT PROBABLY WOULD.
04 BUT -- BUT THE POINT THAT I WAS MAKING, AND
05 AT LEAST THE LEVEL OF OUR UNDERSTANDING TODAY, IS THAT
06 WE'RE NOT ABLE TO DETECT A -- A DIFFERENCE IN RESPONSE
07 THAT WOULD SUGGEST THAT THE ORGANIC FRACTION IS PLAYING A
08 ROLE IN THIS HIGH-DOSE-RESPONSE IN RATS. SO I DO NOT --
09 DR. SEIBER: SO IT'S OVERWHELMED THEN BY THE
10 PARTICLE EFFECT. IS THAT WHAT YOU'RE SAYING?
11 DR. MAUDERLY: IT'S EITHER OVERWHELMED OR IT'S NOT
12 THERE.
13 DR. SEIBER: ALL RIGHT. IT'S NOT THERE.
14 DR. MAUDERLY: I DON'T KNOW. D.N.A. ADDUCT STUDIES
15 HAVE SHOWN THAT THERE ARE D.N.A. -- SIMILAR D.N.A. ADDUCT
16 INCREASES BY PARTICLES WITH AND WITHOUT ORGANICS, AND
17 THOSE ARE INCREASES IN ADDUCTS THAT EXIST NORMALLY. SO
18 THAT -- THAT -- WE THOUGHT THAT WOULD RESOLVE THE ISSUE,
19 BUT IT HASN'T RESOLVED THE ISSUE.
20 BUT THAT DOES NOT MEAN -- I MEAN, THAT DOES
21 NOT PROVE THAT THE -- THAT THERE NOT RISK FROM THAT
22 ORGANIC FRACTION IN HUMANS. IT JUST STRONGLY SUGGESTS,
23 CONVINCINGLY TO ME, THAT THAT FACTOR IS NOT PLAYING A ROLE
24 IN THE HIGH-DOSE RAT RESPONSE.
25 DR. SEIBER: THANK YOU.
0073
01 DR. FROINES: BUT THAT'S NOT ENTIRELY TRUE, JOE,
02 WHEN YOU TAKE INTO ACCOUNT NITRO P.A.H. ADDUCTS. THAT
03 THERE ARE ADDUCTS THAT'S ARE ASSOCIATED -- THAT ARE NOT
04 THE, QUOTE, "TYPICAL ADDUCTS," THAT YOU'RE TALKING ABOUT.
05 DR. MAUDERLY: THERE'S ONLY ONE STUDY THAT I KNOW
06 THAT THOUGHT THEY IDENTIFIED AN ADDUCT THAT MIGHT NOT BE
07 WHAT RANDERATH (PHONETIC) WOULD CALL AN "I" COMPOUND OR
08 THE NORMAL SPOTS, IF YOU WERE, AND THAT WAS A GERMAN STUDY
09 AND I -- AND THERE'S BEEN NO FOLLOW UP ON THAT. I DON'T
10 KNOW WHAT THE STATUS OF THAT IS.
11 BUT IN THE OTHER STUDIES THAT HAVE BEEN DONE,
12 THERE ARE A CLEAR INCREASE IN ADDUCTS, ALTHOUGH THAT THERE
13 IS NOT A PROGRESSIVE DOSE-RELATED INCREASE, BUT THE
14 INCREASES ARE IN BULKY ADDUCTS THAT ARE -- THAT ARE
15 REPRESENTED NORMALLY.
16 BUT CLEARLY THERE ARE -- THERE ARE COMPOUNDS
17 IN DIESEL EXHAUST THAT -- THAT ARE VERY PLAUSIBLE TO INCUR
18 RISK FROM -- FROM D.N.A. DAMAGE. THAT'S NOT MY POINT AT
19 ALL.
20 DR. FROINES: LET ME -- LET ME STOP EVERYONE. PAUL
21 HAD A QUESTION AND KATHIE DID. WERE THERE OTHER QUESTIONS
22 FOR JOE OR BARBARA? PETER HAD ONE, THE STAFF HAD ONE, AND

23 I HAVE ONE.
24 WE HAVE TOO MANY QUESTIONS, AND WE ARE
25 ALREADY FINISHED OUR BREAK WITHOUT HAVING TAKEN IT.

0074

01 SO SOME -- I THINK WHAT I'M GOING TO HAVE TO
02 DO IS EXERCISE SOME LEADERSHIP HERE, AND I THINK WE'LL
03 TAKE OUR BREAK, AND WE'LL JUST HAVE TO GET TO THESE
04 QUESTIONS AS THE DAY PROGRESSES SOMEHOW.
05 I THINK THAT THERE ARE SOME IMPORTANT ISSUES,
06 AND I THINK THE QUESTIONS NEED TO BE ASKED, BUT WE'LL TRY
07 AND FILTER THEM IN. AND SO PEOPLE WHO HAVE QUESTIONS,
08 WOULD YOU WRITE THEM DOWN BECAUSE AS THE DAY GOES ALONG
09 YOU MAY FORGET. BUT I THINK FOR NOW WE SHOULD TRY AND
10 STICK ON SCHEDULE, AND WE'LL TAKE A 15-MINUTE BREAK, AND
11 WE'LL BE RUNNING A LITTLE BIT LATE.
12 AND EVERY SPEAKER SHOULD BE AWARE THAT WE'RE
13 RUNNING A LITTLE BIT LATE NOW. SO LET'S TRY AND STAY
14 WITHIN THE 15- TO 20-MINUTE GUIDELINES, AND SO LET'S TAKE
15 A BREAK. AND BILL SAYS THAT IT'S THROUGH THIS DOOR; IS
16 THAT CORRECT? I DON'T KNOW WHAT YOU MEAN WHEN YOU JUST
17 SHAKE YOUR FINGER. PUT IT INTO WORDS. THERE'S COFFEE
18 BEHIND THAT DOOR. OH, PARDON ME, IT'S A -- IT'S FOR THE
19 PANEL AND SPEAKERS. AND IT'S THE REST OF YOU WILL HAVE TO
20 GO TO THE FIRST FLOOR AND FIND MACHINES AND MAKE DO THE
21 BEST YOU CAN. SORRY.
22 (BREAK)
23 DR. FROINES: OKAY. THERE ARE CONSIDERABLE
24 QUESTIONS. IF WE DON'T GET TO THOSE QUESTIONS SOMEHOW, WE
25 WILL DEFINITELY GET TO TRY AND GET ANSWERS TO THEM BETWEEN

0075

01 NOW AND APRIL. AND I'M HOPING WE CAN GET TO EVERYTHING
02 TODAY. BUT WE'LL JUST HAVE TO SEE HOW TIME PROGRESSES.
03 OUR NEXT SPEAKER -- AND THIS BEGINS THE
04 SECTION ON EPIDEMIOLOGY, IS -- OUR FIRST SPEAKER IS
05 ERIC GARSHICK, WHO IS ERIC GARSHICK M.D., WITH A MASTER OF
06 OCCUPATIONAL HEALTH. ERIC WAS, AS YOU REMEMBER, THE LEAD
07 IN THE EARLIER RAILROAD STUDY, AND HE IS CURRENTLY AT THE
08 VETERAN'S AFFAIRS MEDICAL CENTER IN WEST ROXBURY,
09 MASSACHUSETTS, AND SO WITH NO FURTHER INTRODUCTION, ERIC.
10 DR. GARSHICK: THANK YOU. THANK YOU, JOE. THANK
11 YOU FOR INVITING ME.
12 AND THIS IS, AGAIN, A VERY LARGE DOCUMENT,
13 AND I'VE REVIEWED AS BEST AS I CAN IN THE TIME AVAILABLE,
14 THE SECTION OF THE DOCUMENT THAT WERE RELEVANT TO HUMAN
15 EPIDEMIOLOGY AND THE RISK ASSESSMENT.
16 SO AN OVERVIEW OF WHAT I'M GOING TO TALK
17 ABOUT TODAY IS OTHER GAPS IN THE EPIDEMIOLOGIC STUDIES,
18 WHAT ARE THE LIMITATIONS OF THESE STUDIES FOR RISK
19 ASSESSMENT, AND WHAT OTHER RESEARCH NEEDS, BOTH IN THE
20 RAILROAD WORKER COHORT AND OTHER STUDIES.
21 NOW, WHAT ARE THE RESULTS OF THE
22 EPIDEMIOLOGIC STUDIES? AND THERE WERE THE INCREASE RISK
23 OF LUNG CANCER IN WORKERS WHOSE JOB TITLES INDICATE THERE
24 HAS BEEN OCCUPATIONAL EXPOSURE. AND THE RELATIVE RISK
25 APPEARS TO BE IN THE 1.2 TO 1.5 RANGE, OR 20 TO 50 PERCENT

0076

01 EXCESS AND TO MAKE THE CONSISTENT FINDING IN VARIOUS

02 STUDIES IN DIFFERENT OCCUPATIONAL GROUPS AS SUMMARIZED
03 IN VARIOUS META-ANALYSES, AND I THINK THAT IS A -- PEOPLE
04 GENERALLY AGREE WITH THESE FINDINGS.

05 NEXT SLIDE, PLEASE.

06 SO HOWEVER, FOR STUDIES OF LUNG CANCER, A
07 LATENCY PERIOD OF AT LEAST 10 YEARS OR MORE, AND
08 PREFERABLY GREATER THAN EQUAL 20 YEARS IS DESIRABLE IN
09 STUDYING THE EFFECT OF AN EXPOSURE SINCE THE EFFECT OF A
10 CARCINOGEN IN LUNG CANCER RATES IS NOTED MANY YEARS AFTER
11 FIRST EXPOSURE.

12 AND THERE IS A GAP IN THESE LITERATURE
13 CONCERNING THIS, AND FEW STUDIES IN DIESEL LITERATURE HAVE
14 CLEARLY REPORTED AN OCCURRENCE OF LUNG CANCER AFTER
15 20 YEARS OR MORE WELL-DOCUMENTED EXPOSURE. AND IT'S
16 REALLY NOT A FAULT OF ANY OF THE AUTHORS. IT'S JUST NOT
17 BEEN POSSIBLE TO DO THIS BECAUSE IN GENERAL WHEN DIESELS
18 WERE INTRODUCED DURING THE -- DURING THE 1950'S IN THIS
19 COUNTRY.

20 AND WE'VE -- I'VE IDENTIFIED SEVEN STUDIES
21 THAT SEEM TO HAVE PRESENTING RESULTS OF WORKERS EXPOSED
22 20 OR MORE YEARS. I KNOW THE STAFF IDENTIFIED SIX
23 STUDIES, BUT THERE IS POSSIBLY A SEVENTH.

24 NEXT SLIDE, PLEASE.

25 NOW, FIRST OF ALL IN OUR STUDIES, THIS SLIDE
0077

01 SHOWS THE -- THE RATE THAT THE RAILROAD INDUSTRY CONVERTED
02 FROM STEAMED DIESEL LOCOMOTIVES BETWEEN 1946 AND 1959.

03 IN 1952, ROUGHLY 55 PERCENT OF THE
04 LOCOMOTIVES WERE DIESEL POWERED, AND BY 1959, NEARLY ALL
05 THE LOCOMOTIVES WERE DIESEL.

06 THEREFORE, GOING BACK TO 1959, BY ABOUT 1952,
07 ROUGHLY ONLY ABOUT HALF THE COHORT WOULD HAVE BEEN EXPOSED
08 TO DIESEL FUMES ON AVERAGE.

09 NEXT SLIDE, PLEASE.

10 THE SIMPLEST WAY OF LOOKING AT THE RESULTS OF
11 THE RETROSPECTIVE COHORT STUDY, PARTICULARLY GIVEN THE
12 LIMITATIONS IN THE EXPOSURE BEFORE 1959 IS TO EXAMINE THE
13 RELATIONSHIP BETWEEN JOB CATEGORY IN 1959 AND LUNG CANCER
14 MORTALITY THROUGH 1976.

15 AND THIS -- THE REASON WHY WE CHOSE 1976 IN
16 THIS PRESENTATION TODAY IS THE FACT THERE WERE
17 CONSIDERABLE NUMBER OF MISSING DEATH -- DEATH --
18 UNDERASCERTAINMENT OF DEATHS IN YEAR 1977 THROUGH 1980,
19 AND THE WORKERS WHO ARE THE YOUNGEST IN 1959, AND THIS IS
20 THE RELATIVE RISK OF WORKING IN A DIESEL-EXPOSED JOB,
21 RELATIVE TO NOT WORKING IN A DIESEL-EXPOSED JOB IN THE
22 GROUPS SELECTED FOR STUDY IN THE COHORT, AND THESE
23 WORKERS, 1959, WOULD HAVE HAD THE GREATEST OPPORTUNITY TO
24 HAVE FUTURE DIESEL EXPOSURE THROUGH 1976; WHEREAS IF YOU
25 WERE OLDER IN 1959, YOU WOULD HAVE HAD LESS YEARS OF

0078
01 FUTURE EXPOSURE AHEAD OF YOU.

02 AND A BASIS FOR SELECTING JOB CATEGORY IN
03 1959 IS THAT THE JOB CATEGORIES IN THE RAILROAD INDUSTRY
04 TEND TO BE RELATIVELY STABLE. AND A JOB IN 1959 WOULD
05 HAVE BEEN PREDICTIVE OF FUTURES JOBS.

06 AND SO THE ADJUSTING FOR ATTAINED AGE AND

07 CALENDAR YEAR USING POISSON REGRESSION MODELS, THE OLDER
08 WORK -- THE YOUNGER WORKERS WOULD HAVE HAD AN INCREASED
09 RELATIVE RISK OF DYING OF LUNG CANCER THROUGHOUT THE
10 FOLLOW-UP PERIOD OF 1959 TO 1976 WITH LESSER RISKS THAN
11 THE WORKERS WHO WOULD HAVE HAD LESS CHANCE FOR EXPOSURE,
12 AND THIS IS QUITE SIMILAR TO OUR PUBLISHED INFORMATION
13 WITH MORTALITY THROUGH 1980.

14 NEXT SLIDE PLEASE.

15 NOW, WHEN DIVIDED BY SPECIFIC OCCUPATIONAL
16 GROUPS IN JOB -- BASED ON JOB TITLE IN 1959, THE
17 ENGINEERS, AND FIREMEN, BRAKEMEN, CONDUCTORS, AND SHOP
18 WORKERS, ONE CAN SEE STILL WITH FOLLOW UP THROUGH 1976,
19 THAT THE WORKERS WHO ARE YOUNGER IN 1959 HAD THE GREATEST
20 RISK OF -- INCREASED RISK OF DYING OF LUNG CANCER, THESE
21 STARS ARE P-VALUES THAT I LEFT IN .05, AND THE POINT
22 ESTIMATES HERE THOUGH ARE GENERALLY HIGHER THAN THE
23 LOWER -- THE WORKERS WHO WERE YOUNGER, AND WITH SOME --
24 SOME -- THIS IS SLIGHTLY HIGHER, AND IT'S POSSIBLY THAT
25 THAT REPRESENTS, JUST I MEAN, INACCURACY IN THE EXPOSURE

0079

01 HISTORIES WHERE THAT WE'RE USING JOB TITLES HERE FOR
02 EXPOSURE, BUT IN GENERAL IT LOOKED LIKE THE YOUNGER
03 WORKERS HAD -- HAD THE HIGHER RISK.

04 A LOT OF THEM MADE ABOUT THE SHOP WORKER
05 GROUP WHERE THESE WORKERS DID HAVE HIGHER LEVELS OF
06 EXPOSURE BASED ON OUR SAMPLING; HOWEVER, THE WORKERS
07 SELECTED FOR INCLUSION, THE JOB TITLES WERE VERY GENERAL
08 JOB TITLES, AND THESE WORKERS WORKED IN OTHER NONDIESEL
09 SHOPS. SO THE EFFECT WOULD BE DILUTED OF ANY POSSIBLE
10 EFFECT OF DIESEL EXPOSURE.

11 NEXT SLIDE PLEASE.

12 NOW, IN THE CASE CONTROL STUDY, DEATHS WERE
13 COLLECTED BETWEEN 1981, 1982, OVER 12 MONTHS, AND WORKERS
14 WITH -- WHO WERE -- CASES WITH LUNG CANCER WHO WERE LESS
15 THAN 64 AT DEATH IN THE SERIES WHERE THERE WERE
16 MATCHED TO TWO CONTROLS, THEY HAD INCREASED RELATIVE ODDS
17 OF DYING OF LUNG CANCER OF 1.41 WITH 20 YEARS OF EXPOSURE
18 COUNTING YEARS OF EXPOSURE STARTING IN 1959.

19 RECOGNIZING THAT EXPOSURE CATEGORIES -- AFTER
20 1959 WITH A SURROGATE FOR PRE-1959 EXPOSURE. AND USING
21 THE SAME WAY OF CLASSIFYING EXPOSURE WITH CASES GREATER
22 THAN 65 AT DEATH, THERE WAS NO ELEVATED RISK DUE TO WORK
23 IN A DIESEL-EXPOSE JOB, AND THESE RESULTS WERE ADJUSTING
24 FOR CIGARETTE SMOKING USING NEXT OF KIN CIGARETTE SMOKING
25 HISTORIES.

0080

01 NEXT SLIDE, PLEASE.

02 SO -- SO IN OUR STUDY, EVEN THOUGH THERE IS
03 SOME INACCURACIES OF CATEGORIZING EXPOSURE BEFORE 1959, WE
04 DID HAVE WORKERS WITH MORE THAN 20 YEARS' EXPOSURE.

05 THE SECOND STUDY THAT LOOKS AT WORKERS WITH
06 MORE THAN 20 YEARS' EXPOSURE WAS PUBLISHED BY STEENLAND
07 AND CO-WORKERS, THEY ARE A TEAMSTERS UNION STUDY. AND
08 THEY FACE THE SAME LIMITATIONS THAT WE DID; THAT DIESEL
09 TRUCKS ARE GRADUALLY INTRODUCED IN THIS COUNTRY IN THE
10 1950'S AND EARLY 1960'S, WHEREAS IN THE LARGE COMPANIES
11 WERE LARGELY CONVERTED TO DIESEL BY 1960. AND THE DEATHS

12 WERE COLLECTED -- THE 1982 TO 1983.

13 SO AGAIN, ROUGHLY A LITTLE MORE THAN 20-YEAR
14 FOLLOW UP WHEN MOST OF THE COHORT WOULD HAVE BEEN EXPOSED.
15 THE POTENTIAL FOR OTHER WORKERS SOME, RATHER, DRIVERS AND
16 MECHANICS TO BE EXPOSED TO DIESEL BEFORE THEN DEPENDING ON
17 THE -- WHEN THEIR TRUCKING COMPANY CONVERTED TO DIESEL.
18 ALTHOUGH THAT WAS NOT SPECIFICALLY KNOWN IN THE STUDY.

19 BY USING TEAMSTER JOB HISTORY RECORDS, IF YOU
20 LOOKED AT LONG-HAUL DRIVERS WITH MORE THAN 20 YEARS OF
21 TEAMSTER MEMBERSHIP, THERE WAS AN INCREASED POINT ESTIMATE
22 OF THE RELATIVE ODDS OF THE LUNG CANCER. IF ONE LOOKED AT
23 THOSE WORKERS -- AND IT WAS INCREASED -- INCREASING RISK,
24 BUT INCREASING YEARS OF WORK.

25 IF ONE LIMITED WORK HISTORY TO THOSE WORKING

0081

01 AFTER 1959, THOSE WITH MORE THAN 18 YEARS OF EXPOSURE ALSO
02 HAD AN ELEVATED RISK. AND THESE WERE ADJUSTED FOR
03 SMOKING. AND THESE STUDIES I'M QUOTING HERE, THIS STUDY
04 AND OUR STUDY IS THE ONLY STUDIES THAT HAD EXPOSURE
05 CHARACTERIZED BY -- BY SAMPLING, AIR SAMPLING.

06 NEXT SLIDE, PLEASE.

07 NOW, WHAT ABOUT THE LEVELS IN THE TEAMSTER
08 UNION STUDY, AND THIS -- THESE LEVELS WERE COLLECTED SOME
09 TIME IN THE MID 1980'S BEST AS I CAN TELL FROM THEIR
10 PAPERS, AND THIS SLIDE TALKS ABOUT WHAT THE OVERALL RISK
11 WAS FOR LONG-HAUL DRIVERS, SHORT-HAUL DRIVERS. THESE
12 DRIVERS WOULD HAVE DRIVEN DIESEL TRUCKS, THESE DRIVERS
13 WOULD HAVE DRIVEN GASOLINE TRUCKS, MECHANICS, RELATIVE --
14 R.R. IS RELATIVE RISK -- TRUCK MECHANICS, LOADING DOCK
15 WORKERS, AND RESULTS OF SAMPLING DONE ALONG THE HIGHWAYS
16 AND RESIDENTIAL SAMPLES.

17 AND THEY SAMPLED FOR ELEMENTAL CARBON, AND
18 THEN THESE ARE OUR VALUES USING DATA IN THEIR PAPER THAT
19 CAN CONVERT THEM TO RESPIRABLE PARTICLES THAT WE'RE MORE
20 USED TO SEEING AND INTERPRETING LEVELS IN THIS RANGE.

21 AND YOU CAN SEE THAT -- YOU KNOW, A SAMPLING
22 DONE A GOOD -- OVER 20 YEARS AFTER THESE PEOPLE WERE
23 PROBABLY EXPOSED TO THE EXPOSURE: THE LEVELS EXPERIENCED
24 BY TRUCK DRIVERS WERE IN THE RANGE OF 26, 25 MICROGRAMS
25 PER CUBIC METER; THE SHORT-HAUL DRIVERS HAD SIMILAR

0082

01 LEVELS, EVEN THOUGH THEY WEREN'T REALLY DRIVING DIESEL
02 TRUCKS; MECHANICS HAD THE HIGHEST LEVELS WITH AN ELEVATED
03 RELATIVE RISK; THE DOCK WORKERS, THE LOADING DOCK WORKERS
04 HAD ELEVATED LEVELS OF RESPIRABLE PARTICULATE, BUT HAD NOT
05 BEEN WORKING LONG ENOUGH TO SEE AN EFFECT PROBABLY.

06 THE DIESEL -- THE FORK -- THE EXPOSURE IS
07 BLAMED ON FORK-LIFT TRUCKS, AND THESE HAVE BEEN RECENTLY
08 INTRODUCED -- MORE RECENTLY INTRODUCED. RATHER, DIESEL
09 FORK-LIFT TRUCKS HAVE BEEN RECENTLY INTRODUCED.

10 HIGHWAY LEVELS WERE 17 MICROGRAMS PER CUBIC METER,
11 AND THIS SUGGESTED THAT PERHAPS MOST OF THE EXPOSURE HAD
12 COME FROM THE HIGHWAY RATHER THAN THE PARTICULAR TRUCK THE
13 DRIVER WAS DRIVING, EXPLAINING THESE -- THIS INFORMATION.

14 AND RESIDENTIAL LEVELS WERE -- WERE MUCH
15 LOWER.

16 THIS IS QUITE INTERESTING IF, IN FACT, THESE

17 LEVELS ARE RESPONSIBLE FOR INCREASE IN LUNG CANCER, IN
18 THAT IT -- YOU KNOW, IT SUGGESTS THAT DIESEL MAY BE
19 CONTRIBUTING TO SOME OVERALL ENVIRONMENTAL POOL. BUT
20 AGAIN, WE ARE LIMITED BY NOT KNOWING THE HISTORICAL LEVELS
21 OF EXPOSURE IN THESE -- IN THESE DRIVERS.
22 THERE ARE FOUR ADDITIONAL STUDIES THAT AREN'T
23 ACCOMPANIED BY EXPOSURE INFORMATION WHERE WORKERS WITH
24 MORE THAN 20 YEARS OF EXPOSURE HAVE AN ELEVATED RISK OF
25 LUNG CANCER, ALTHOUGH THESE ARE MUCH WEAKER STUDIES AND
0083 MUCH WEAKER WHERE THE EXPOSURE THE HISTORY IS NOT QUITE
01 AS -- QUITE AS WELL SORTED OUT. SO NOW, I'LL NOT REVIEW
02 THOSE HERE FOR TIME CONSTRAINTS.
03
04 SO THE CONSISTENCY OF THESE RESULTS SUGGESTS
05 THAT THE RESULTS ARE LIKELY TO BE EXPOSED -- EXPLAINED BY
06 EXPOSURE TO DIESEL EXHAUST AND NUMEROUS BODIES HAVE
07 PRESENTED A STATEMENT WORDED SIMILARLY TO THIS ONE ON THE
08 SLIDE.
09 AND IN THE -- I LOOKED AT THE WAY THE STAFF
10 HAS WORDED THEIR QUALITATIVE COMMENT, AND IT'S QUITE
11 SIMILAR TO THE COMMENTS OF H.E.I., W.H.O., AND I.A.R.C.
12 AND YOU KNOW, THIS OVERALL CONCLUSION BASED ON WHAT'S IN
13 THE EPIDEMIOLOGY IS NOT IN LINE WITH OTHER BODIES.
14 HOWEVER, THE MOST IMPORTANT FACTORS THAT
15 LIMIT THE USE OF MORE DEFINITIVE LANGUAGE IS THE LACK OF
16 THE ABILITY TO LINK ACTUAL EXPOSURE TO OUTCOME IN STUDIES
17 OF WORKERS WITH WELL-DOCUMENTED EXPOSURE OVER 20 TO 30
18 YEARS OR MORE, GIVEN WHAT WE KNOW ABOUT HUMAN LUNG CANCER
19 BIOLOGY.
20 AND FOR RISK ASSESSMENT, AN ASSESSMENT OF
21 HISTORICAL EXPOSURE NEEDS TO BE AVAILABLE TO TRY TO LINK
22 ACTUAL LEVEL EXPOSURE TO CANCER OUTCOME.
23 NEXT SLIDE, PLEASE.
24 SO WHAT ABOUT THE RAILROAD WORKER
25 EXPOSURE-RESPONSE RELATIONSHIPS? IN PUBLISHED PAPERS, WE
0084 INITIALLY STARTED COUNTING EXPOSURE AT 1959 BECAUSE OF THE
01 UNCERTAINTY OF PREDICTING WHO ACTUALLY WAS EXPOSED BEFORE
02 1959.
03
04 WE CURRENTLY BELIEVE THAT ACCOUNTING FOR
05 EXPOSURE BEFORE 1959 IS IMPORTANT IN UNDERSTANDING THE
06 EXPOSURE-RESPONSE RELATIONSHIP IN THIS -- IN THIS COHORT.
07 NEXT SLIDE, PLEASE.
08 NOW, THERE IS SOME SPECIFIC COMMENTS ABOUT
09 THE DOSE-RESPONSE ANALYSES PRESENTED IN THE -- IN THE
10 DOCUMENT. THIS IS BASED ON THE CASE CONTROL STUDY, AND IN
11 THE DOCUMENT, AS FAR AS I CAN TELL, THE RISK OF LUNG
12 CANCER -- THE RISK OF LUNG CANCER ESTIMATED FROM OUR PAPER
13 WAS ASSUMED TO INCREASE OVER 20 YEARS BASED ON OUR
14 REGRESSION RESULTS. AND THIS IS WHAT WAS USED TO ESTIMATE
15 THE RISKS OF OVER 20 YEARS OF EXPOSURE IN THE CASE CONTROL
16 STUDY IN THE DOCUMENT.
17 HOWEVER, BECAUSE OF THE 1959 EXPOSURE --
18 EXPOSURE BEFORE 1959, THE RISK ACTUALLY ACCUMULATED OVER
19 20 TO 30 YEARS, DEPENDING ON THE LIKELIHOOD THAT WORKER
20 WAS EXPOSED, WHICH OF COURSE, WE'RE -- FOR INDIVIDUAL
21 WORKER, UNCERTAIN OF.

22 THEREFORE, IN THE DOCUMENT, THE CALCULATED
23 SLOPE MAY THEN OVERESTIMATE THE RISK BASED ON THE RISK
24 ASSESSMENT BASED ON CASE CONTROL DATA.
25 NEXT SLIDE, PLEASE.

0085

01 NOW, GOING TO THE COHORT STUDY. THIS GRAPH
02 ILLUSTRATES THE RELATIONSHIP BETWEEN OBSERVED OVER
03 EXPECTED DEATHS WITH YEAR OF DEATH IN THE RETROSPECTIVE
04 COHORT STUDY WITH INITIALLY THE OBSERVED OVER EXPECTED
05 DEATHS STARTING AT ABOUT .08 -- .8, RATHER, CONSISTENT
06 WITH THE HEALTHY-WORKER EFFECT, AND THEN AS THE WORKERS
07 AGE, THE OBSERVED OVER EXPECTED RATES BASED ON U.S.
08 NATIONAL RATES BECOMING ABOUT 1. AND CAN YOU SEE THEN IN
09 ABOUT 1977 THE RATES DROPPING OFF, SUCH THAT BY 1980, THE
10 RATIO OF OBSERVED TO EXPECTED IS ROUGHLY ABOUT .3, AND FOR
11 THIS REASON, WE'VE -- WE AGREE IT'S IMPORTANT TO TRUNCATE
12 FOLLOW UP WITH THIS COHORT IN 1976.

13 HOWEVER, YOU CAN ALSO SEE IF ONE WAS EXPOSED
14 AT ABOUT THIS TIME PERIOD, 1959 OR BEFORE, YOU WOULD LIKE
15 TO BE LOOKING AT ABOUT HERE TO SEE EVIDENCE OF SOME -- OF
16 SOME RESPONSE, AND UNFORTUNATELY, WE CAN'T -- WE CAN'T DO
17 THAT ACCURATELY.

18 NEXT SLIDE, PLEASE.

19 NOW, IN THE FIVE-YEAR LAG MODELS IN OUR
20 PUBLISHED WORK AND OUR WORK DONE BY A.R.B. AND DR. CRUMP,
21 A MODEL OF EXPOSURE WAS ADAPTED THAT IGNORES EXPOSURE IN
22 THE YEAR OF DEATH IN THE PRECEDING FOUR YEARS AS
23 CONTRIBUTING TO MORTALITY. AND IF YOU LOOK AT THE GROUP
24 IN OUR WORK AND WORK TALKED ABOUT IN THE DOCUMENT, WITH
25 THE MOST EXPOSURE POSSIBLE, COUNTING AFTER 1959, WITH 15

0086

01 TO 17 YEARS' EXPOSURE, THESE DEATHS ONLY COULD HAVE
02 OCCURRED IN 1978 TO 1980. REALLY ONLY, YOU KNOW, A VERY
03 FEW CELLS IN THE FIRST YEARS OF FOLLOW UP.

04 THEREFORE THE MISSING DEATHS IN 1977 AND
05 1980, AGAIN, PRECLUDE AN ACCURATE RISK ASSESSMENT USING
06 DEATHS IN THESE YEARS, AND WE'RE GLAD THEY'VE BEEN
07 EXCLUDED.

08 HOWEVER, THESE YEARS OF FOLLOW UP ARE
09 IMPORTANT FOR RISK ASSESSMENT BECAUSE THE WORKER WHO HAS
10 THE GREATER DURATION OF EXPOSURE WOULD BE EXPECTED TO HAVE
11 DEATH IN THESE YEARS.

12 NEXT SLIDE, PLEASE.

13 NOW, JUST SOME SPECIFIC QUESTIONS I HAD ABOUT
14 SOME OF THE ANALYSES PRESENTED IN THE PAPER REGARDING THE
15 COHORT STUDY EXPOSURE-RESPONSE.

16 YOU KNOW, IN REGARDS TO THE MODELING OF RISK,
17 WE STILL FEEL THAT THE USE OF FIVE-YEAR AGE -- ATTAINED
18 AGE CATEGORIES IS MORE DESIRABLE THAN TEN-YEAR AGE
19 CATEGORIES, RATHER THAN AGE IN 1959, AND THE USE OF
20 TEN-YEAR AGE CATEGORIES IS USED IN THE DOCUMENT.

21 THERE'S A FIGURE 7-3, WHICH RELATES YEARS OF
22 EXPOSURE TO RELATIVE RISK, SHOWING A POSITIVE
23 DOSE-RESPONSE, AND WE'RE WONDERING IF ACTUALLY GIVEN THE
24 NUMBER OF YEARS THAT'S LISTED AS EXPOSURE, 25 YEARS,
25 WHETHER -- RATHER THAN THE -- WHETHER EXPOSURE ACTUALLY

0087

01 STARTED IN 1952 TO 1959 AS INDICATED ON THE GRAPH, AND
02 WE'RE ALSO WONDERING AT THE SAME POSITIVE DOSE-RESPONSE
03 RELATIONSHIP WOULD HAVE BEEN FOUND IF FIVE-YEAR AGE
04 CATEGORIES WERE USED TO ADJUST FOR AGE.

05 AND THE OTHER COMMENT IS THAT IT LOOKS LIKE
06 EXPOSURE ACCUMULATED -- EXPOSURE WAS STARTING TO BE
07 ACCUMULATED IN 1952, RATHER THAN BEFORE 1952. ALTHOUGH IN
08 THE APPENDIX, EXPOSURE DATING BACK EARLIER IN THE COHORT
09 WE USED IN SOME OF THE ANALYSES, IT'S NOT CLEAR IF A WHOLE
10 YEAR OR A FRACTION OF A YEAR BASED ON PERCENT DIESEL WAS
11 ADDED TO THE EXPOSURE. AND NOT CONSIDERING EXPOSURE
12 BEFORE 1952, THEN WOULD IGNORE EXPOSURE FOR 45 PERCENT OF
13 THE COHORT.

14 NOW, IT WAS LESLIE STAYNER FROM N.I.O.S.H.,
15 WE EXPLORE A MONTE CARLO TO ASSESS THE UNCERTAINTY OF
16 PRE-1959 EXPOSURE.

17 IN THIS GRAPH, WE RANDOMLY ASSIGNED EXPOSURE
18 BASED ON PERCENT DIESEL IN ANY YEAR FOR THOSE WORKERS
19 WHOSE JOB'S STARTING DATE INDICATED THEY WERE WORKING.

20 AND THIS WAS DONE A THOUSAND TIMES, AND FOR
21 EACH SIMULATION A QUASI MODEL WAS FIT STRATIFYING ON
22 ATTAINED AGE IN FIVE-YEAR AGE GROUPS IN A CALENDAR YEAR,
23 AND DIVIDED THE YEARS OF FOLLOW UP INTO -- INTO
24 CATEGORIES.

25 AND WHEN WE LOOK AT EXPOSURE IN THIS WAY,
0088

01 THIS IS THE ZERO TO 7 YEARS, 7 TO 11 YEARS, 11 TO 14
02 YEARS, 14 TO 18 YEARS, AND GREATER THAN 18 YEARS, THE
03 SLOPE LOOKING -- LOOKING AT YEARS OF EXPOSURE APPEARS
04 RELATIVELY FLAT, WHEREAS IF YOU WOULD MODEL YEARS OF
05 EXPOSURE USING A CONTINUOUS VARIABLE STARTING FROM ZERO
06 YEARS, THE REGRESSION LINE APPEARS TO BE ANCHORED IN ZERO,
07 JUST GIVING A POSITIVE SLOPE.

08 SO WE ARE -- WE ARE JUST SHOWING THIS TO
09 POINT OUT THE UNCERTAINTIES OF THE ANALYSES AND OF
10 ASSIGNING THE SLOPES TO THESE DATA WITH CONFIDENCE AT THIS
11 TIME.

12 NEXT SLIDE, PLEASE.

13 NOW, WHAT ABOUT RAILROAD WORKERS HISTORICAL
14 ASSESSMENT, AND JUST TO GO THROUGH THIS RELATIVELY
15 QUICKLY, WE'VE IDENTIFIED -- IT'S VERY IMPORTANT TO
16 IDENTIFY WHEN THESE WORKERS STARTED -- DIESEL EXPOSURE
17 ACTUALLY STARTED.

18 AND THERE ARE HISTORICAL RECORDS ABOUT THE
19 TRANSITION TO DIESEL AND A CHANGE IN ROSTER THE RAILROADS
20 OVER TIME THAT ARE AVAILABLE. WE HAVE ACTUALLY ON DATA
21 TAPE THE LAST RAILROAD EMPLOYER AVAILABLE. AND THAT
22 WOULD PERMIT ESTIMATION OF THE START DATE OF EXPOSURE FOR
23 WORKERS.

24 WE'VE ALSO IDENTIFIED RECORDS DESCRIBING
25 EMISSION FACTORS AND FUEL CONSUMPTION FOR VARIETY OF
0089

01 ENGINES THAT MIGHT PERMIT A BETTER ESTIMATION OF
02 HISTORICAL EXPOSURES, AND THIS IS ONE WAY OF GETTING A
03 BETTER HANDLE ON RAILROAD EXPOSURE IN THE PAST.

04 NEXT SLIDE, PLEASE.

05 SO WHAT ARE THOSE LIMITATIONS? THE DEATH

06 INFORMATION AVAILABLE FOR 1976 AND FOLLOW UP WOULD IMPROVE
07 THE DESCRIPTION ON THE EXPOSURE-RESPONSE RELATIONSHIP WITH
08 MORE CONFIDENCE. THERE IS UNCERTAINTY OF THE EXPOSURE
09 ASSIGNMENTS PRE-1959, AND NO HISTORICAL MEASUREMENTS WERE
10 AVAILABLE, BUT THERE MAY BE A WAY OF DEALING WITH THIS.
11 AND CURRENTLY, THERE IS NO SPECIFIC MARKER OF EXPOSURE
12 MEASURED. THIS MIGHT BE SOLVED BY GOING BACK TO THE
13 RAILROADS AND DOING SOME ADDITIONAL SAMPLING USING THE
14 OLDER METHODS IN SAMPLING FOR ELEMENTAL CARBON.
15 LAST SLIDE, PLEASE.
16 SO WHAT ARE THE RESEARCH NEEDS? ONE IS TO
17 ASSESS THE LUNG CANCER RISK OVER A LONG PERIOD OF EXPOSURE
18 IN TIME SINCE FIRST EXPOSURE; EFFECTIVE EXPOSURE FROM THE
19 1960'S SHOULD BE DETECTIBLE IN LATE 1980'S AND BEYOND;
20 INCLUDES LARGE NUMBERS OF SUBJECTS OVER RANDOM EXPOSURES
21 TO DESCRIBE RISK; USE STATE OF THE ART EXPOSURE
22 MEASUREMENTS; AND CONDUCT AN EXTENSIVE RETROSPECTIVE
23 EXPOSURE ASSESSMENT TO LINK PERSONAL EXPOSURE TO OUTCOME.
24 THANK YOU.
25 DR. FROINES: WE ARE NOW INTENDING TO BRING
0090
01 TOM SMITH INTO THE PICTURE, LITERALLY.
02 HI, TOM.
03 DR. TOM SMITH: CAN YOU HEAR ME?
04 DR. FROINES: YES.
05 DR. TOM SMITH: OKAY. IT SOUNDED LIKE YOU CAN HEAR
06 ME.
07 DR. FROINES: YES. CAN YOU HEAR US?
08 DR. TOM SMITH: YES. I CAN ACTUALLY EVEN SEE YOU.
09 IT'S A LITTLE BIT WEIRD. I FEEL LIKE THE NEWSCASTER OR
10 SOMETHING. ALL RIGHT.
11 DR. FROINES: YOU HAVE ABOUT 15 MINUTES NOW.
12 DR. TOM SMITH: OKAY. I'LL SKIP TELLING YOU WHAT
13 HERE AND THEREFORE, AND JUST START WITH SAYING WHO I AM
14 AND WHAT I'M DOING.
15 CAN YOU SEE THE PIECE OF PAPER THERE?
16 WHOOPS, JUST A SECOND. THIS HIGH TECH STUFF IS PRETTY --
17 GOT IT. OKAY.
18 MY BACKGROUND IS THAT OF THE CO-INVESTIGATOR
19 WHO WAS IN CHARGE OF THE EXPOSURE ASSESSMENT FOR THE
20 GARSHICK STUDY. I'M THE GUY WHO WAS THE SECOND AUTHOR OF
21 MOST OF THOSE PAPERS. THE PEOPLE WHO WERE THE FIRST
22 AUTHOR DID THE HARD WORK, AND JUSTIFIABLY WERE FIRST.
23 BY WAY OF MY BACKGROUND, I HAVE PERFORMED A
24 LOT OF DIFFERENT EXPOSURE ASSESSMENT STUDIES, AND THERE'S
25 A LIST SHOWN. FOR THOSE WHO MIGHT CARE, I HAVE OVER A
0091
01 HUNDRED PUBLICATIONS, AND MANY OF THOSE AS YOU MIGHT GUESS
02 WERE CO-AUTHORED WITH SUSAN WOSKIE AND KATHIE HAMMOND.
03 WHAT I WANT TO DO IS REALLY TALK ABOUT TWO
04 ASPECTS OF THE RISK ASSESSMENT. I WANT TO TALK A LITTLE
05 BIT ABOUT THE ANIMAL ASPECTS OF THE WORK, AND I OBVIOUSLY
06 WANT TO SAY SOMETHING MORE ABOUT THE APPLICATION OF THE
07 GARSHICK STUDIES TO THE RISK ASSESSMENT.
08 FOR THE ANIMAL WORK, I HAD TWO SPECIFIC AREAS
09 THAT I WAS -- PERHAPS CONCERNED WITH IS A LITTLE TOO
10 STRONG, BUT AS LEAST INTERESTED THAT YOU CONSIDER THEM.

11 THE FIRST WAS THE USE OF THE RATIO OF THE RAT
12 ALVEOLAR DIMENSIONS TO THE HUMAN ALVEOLAR DIMENSIONS, AND
13 THE SECOND ASPECT IS THE MODEL OF DUST OVERLOAD.
14 LOOKING AT -- WELL, NOW, I'LL TALK ABOUT THE
15 GARSHICK STUDY IN A MINUTE.
16 FOR THE FIRST PART OF THE ANIMAL CONCERNS, IT
17 SEEMS TO ME THAT THERE WAS A PROBLEM WITH THE WAY THE RISK
18 ASSESSMENT PRESENTED THE SCALING GOING FROM THE RAT LUNG
19 TO THE HUMAN LUNG.
20 THE GOAL IS REALLY TO LOOK AT THE DOSE AT THE
21 SITE OF ACTION OF THE PARTICULATE, THE DIESEL
22 PARTICULATES. IN THE RATS, THE SITE OF ACTION IS THE
23 ALVEOLI, AND WHAT WAS USED WAS THE RATIO OF THE RAT TO THE
24 HUMAN ALVEOLAR AREA.
25 I'M CONCERNED THAT THIS MAY UNDERESTIMATE THE
0092
01 ACTUAL RATIO OF THE DOSES BECAUSE HUMANS DON'T GET
02 ALVEOLAR TUMORS. THEY GET AIRWAY TUMORS, BRONCHIAL
03 TUMORS. AND AS A RESULT, IT MAY MAKE MORE SENSE TO LOOK
04 AT THE RATIO OF THE RAT ALVEOLI TO HUMAN AIRWAY SURFACE
05 BECAUSE I THINK IN THAT CASE, YOU WILL GET A MORE
06 APPROPRIATE RATIO OF THE -- THE DEPOSITION SITE AND THE
07 TARGET AREA, WHICH WILL RAISE THE RISK RATIO, AND I
08 BELIEVE WILL MAKE IT MORE COMPARABLE TO THOSE SEEN IN THE
09 HUMAN STUDIES.
10 FOR THE MODEL OF DUST OVERLOAD, THERE IS A
11 POST-DOCTORAL FELLOW, WHO IS PERHAPS AN ASSISTANT
12 PROFESSOR NOW IN DR. FROINE'S LABORATORY, BY THE NAME OF
13 R.C. YU, NOT C.P. YU WHO DID THE MODELING WHICH WAS
14 REPORTED ON IN THE DOCUMENT.
15 HE DEVELOPED A MODEL USING WHAT ARE CALLED
16 MC CALLIS MENTEN (PHONETIC) TYPE KINETICS. THE
17 INTERESTING THING ABOUT THIS IS WITH ONE SIMPLE MODEL, HE
18 WAS ABLE TO DESCRIBE THE KINETICS OF THE RATS AND OTHER
19 ANIMALS TO A WIDE VARIETY OF TOXIC MATERIALS.
20 IT'S A MUCH SIMPLER APPROACH THAN WAS USED BY
21 C.P. YU AND INVOLVED THE ESTIMATION OF MUCH FEWER
22 CONSTANTS. SPECIFICALLY, THE OVERLOAD CONDITION I BELIEVE
23 IS -- IS MISREPRESENTED AS A YES-NO KIND OF A CONDITION;
24 THAT IS, YOU EITHER ARE IN OVERLOAD OR NOT.
25 IT MAKES MORE SENSE WHEN YOU LOOK AT THE
0093
01 ANIMAL DATA TO THINK OF IT THAT THE DUST CLEARANCE GETS
02 PROGRESSIVELY SLOWER THE MORE DUST YOU HAVE TOTAL IN THE
03 LUNG, AND WE CAN TALK ABOUT THAT MORE IF SOMEBODY WISHES
04 TO.
05 GOING NEXT TO OUR STUDIES, THE GOAL OF THE
06 APPLICATION OF OUR STUDIES IN THE RISK ASSESSMENT IS TO
07 ESTIMATE THE SLOPE FACTOR; THAT IS TO SAY, HOW MUCH RISK
08 DO YOU GET PER UNIT OF EXPOSURE.
09 THE CURRENT DOCUMENT HAS EXTENSIVE
10 DISCUSSIONS OF THE UNCERTAINTIES OR THE ERROR IN THE
11 MORTALITY SCALE, AND THERE ARE ERROR BARS PROVIDED FOR
12 EACH OF THE POINTS, AS YOU WILL RECALL FROM ERIC'S
13 PRESENTATION JUST A MINUTE AGO.
14 THE PROBLEM IS FROM MY PERSPECTIVE, THERE ARE
15 NO EQUIVALENT ERROR BARS OR UNCERTAINTIES INDICATED FOR

16 THE EXPOSURE SCALE. AND SINCE THE SLOPE, AS I'M SURE YOU
17 ALL KNOW, IS THE RATIO OF RISK OF DISEASE TO EXPOSURE
18 INTENSITY TIMES YEARS -- ASSUMING YOU'RE USING CUMULATIVE
19 EXPOSURE AS YOUR DOSE INDEX -- IT SEEMS TO ME THAT WHILE
20 THE YEARS PART ARE RELATIVELY -- READILY QUANTIFIED, IT'S
21 NOT SO EASY TO QUANTIFY THE EXPOSURE INTENSITY. AND BOTH
22 OF THEM ARE NEEDED TO GIVE A DOSE METRIC.
23 BECAUSE AS -- AS I BELIEVE YOU CAN SEE IN THE
24 MODEL THAT WAS USED -- I CAN'T RECALL THE EXACT NAME FOR
25 IT, WHETHER IT WAS THE ROOF FUNCTION OR THE -- I THINK IT
0094 WAS THE ROOF FUNCTION, THAT SHOWED A UP-AND-DOWN TYPE OF
02 RISK PROFILE.
03 WHAT THAT MEANS IS THAT EACH YEAR OF EXPOSURE
04 DOES NOT CARRY EQUIVALENT RISKS, IF YOU PRESUME THAT IT'S
05 A QUANTITATIVE RELATIONSHIP.
06 THAT SECONDLY, VARIATION IN INTENSITY OCCURS
07 ACROSS TIME, AND THE PROBLEM WITH OUR EXPOSURE ASSESSMENT
08 WAS THAT WE HAVE A NUMBER OF LIMITATIONS OF OUR STUDY, AND
09 THESE HAVE BEEN NOTED BY A LOT OF PEOPLE, AND ARE
10 DISCUSSED TO SOME DEGREE IN THE DOCUMENT.
11 ONE OF THE THINGS THAT MAY NOT BE FULLY CLEAR
12 IS THAT I HAVE NO PROBLEM WITH WHAT WE MEASURED BECAUSE I
13 BELIEVE THOSE NUMBERS ARE QUITE MEANINGFUL AND REPRESENT
14 WHAT WE SAW.
15 THE DIFFICULTY IS THERE WERE A LOT OF THINGS
16 THAT WE DIDN'T MEASURE. WE MADE -- WE HAD NO MEASUREMENTS
17 OF EARLY EXPOSURE CONDITIONS. WE HAD NO MEASUREMENTS OF
18 COMMON EQUIP TYPES, SUCH AS THE FIRST GENERATION OF
19 LOCOMOTIVES, OR EVEN THE THIRD GENERATION OF LOCOMOTIVES.
20 WE MADE NO MEASUREMENTS IN MANY AREAS, AND IN
21 FACT, MOST AREAS OF THE UNITED STATES.
22 WE HAVE NO MEASUREMENTS FROM THE LARGE
23 RAILROADS AS OPPOSED TO THE SMALL RAILROADS, AND IT'S NOT
24 INCONCEIVABLE THAT THERE COULD BE SYSTEMATIC DIFFERENCES
25 BETWEEN THEM.
0095 AS A RESULT, WE HAVE A PROBLEM KNOWING WHAT
01 THE FULL RANGE WAS OF EXPOSURES. WE OBSERVED A RANGE, BUT
02 WE CAN'T SAY WHETHER THIS REPRESENTS THE FULL RANGE. AND
03 AS A RESULT, WE COULD EASILY BE UNDERESTIMATING THE RANGE
04 OR WE COULD BE OVER ESTIMATING IT. AND WE JUST DON'T HAVE
05 ENOUGH INFORMATION TO -- TO SAY.
06 IN CONCLUSION THEN, BECAUSE YOU REALLY WANT
07 PRECISE AND ACCURATE -- READ THAT UNBIASED -- ESTIMATE OF
08 CUMULATIVE EXPOSURE, THE MISSING INFORMATION MEANS YOU
09 CAN'T DO THAT. AND AS A RESULT, I BELIEVE THAT SUITABLE
10 ESTIMATES OF THE SLOPE FACTOR ALSO CANNOT BE MADE.
11 AND SO THE QUESTION OF INTEREST HOW MUCH RISK
12 PER UNIT OF EXPOSURE CAN'T BE ANSWERED AT THIS TIME.
13 THANK YOU VERY MUCH, AND I'LL BE HAPPY TO
14 ANSWER QUESTIONS THAT ANYBODY MIGHT HAVE, WHOEVER IS OUT
15 THERE IN T.V. LAND.
16 DR. FROINES: THANK YOU, TOM.
17 CAN WE GET THE LIGHTS BACK UP AND --
18 DR. TOM SMITH: SURE.
19 DR. FROINES: I ASSUME THAT ALLAN IS GOING TO SHOW

21 SLIDES, OVERHEADS, BUT WE'RE STILL GOING TO NEED THE
22 SCREEN. SO WE HAVE TO MAKE --
23 DR. TOM SMITH: JOHN, WHAT DO YOU WANT ME TO DO?
24 I'M ASSUMING I NEED TO STAY AVAILABLE AND POSSIBLY ANSWER
25 QUESTIONS AND STUFF.

0096
01 DR. FROINES: YEAH, I THINK YOU SHOULD STAY
02 AVAILABLE, BUT WE NEED YOU OFF THE SCREEN.
03 DR. TOM SMITH: THAT'S ALL RIGHT. IT DOESN'T HURT
04 WHEN YOU TAKE ME OFF.
05 DR. FROINES: YOU CAN GO BACK INTO THE MORE
06 WRITER'S CULTURE OF BOSTON AS OPPOSED TO OUR VISUAL
07 LOS ANGELES.
08 DR. TOM SMITH: ALL RIGHT.
09 DR. FROINES: OUR NEXT SPEAKER IS ALLAN SMITH FROM
10 THE UNIVERSITY OF CALIFORNIA AT BERKLEY, WHO IS KNOWN BY
11 EVERYONE I THINK, AND IS CERTAINLY WELL REGARDED IN
12 EPIDEMIOLOGY IN GENERAL, AND IN THIS PARTICULAR AREA IN
13 PARTICULAR. SO ALLAN.
14 DR. ALLAN SMITH: THANK YOU.
15 I MAINLY WANTED TO FOCUS TODAY ON THE ISSUE
16 OF DOES DIESEL CAUSE HUMAN CANCER, AND I THINK IT'S AT THE
17 HEART OF A LOT OF THE ISSUES THAT SURROUND US. AND THEN I
18 WANT TO VERY BRIEFLY PRESENT A SIMPLE APPROACH TO RISK
19 ASSESSMENT BASED ON THE CONCLUSION THAT IT IS A CAUSE OF
20 HUMAN LUNG CANCER.
21 NOW, THIS IS MY FAVORITE ADAPTATION OF THE
22 CRITERIA OFTEN CALLED THE BRADFORD-HILL CRITERIA.
23 WHEN CONSIDERING WHETHER OR NOT AN AGENT
24 CAUSES DISEASE IN HUMAN STUDIES, WE NEED TO CONSIDER
25 WHETHER OR NOT FINDINGS MIGHT BE DUE TO CHANCE. WHETHER

0097
01 THEY MIGHT BE DUE TO SOME SORT OF BIAS. WHETHER THE
02 FINDINGS SHOW SOME CONSISTENCY PATTERN.
03 STRENGTH OF ASSOCIATION CAN HELP US, BUT IN
04 THIS INSTANCE, WE ARE LOOKING FOR AN ASSOCIATION WHICH WE
05 BELIEVE AT PRESENT WOULDN'T BE CHARACTERIZED AS STRONG.
06 IT DOESN'T MEAN TO SAY IT'S NOT REAL, BUT WE DIDN'T USE
07 THE STRENGTH OF ASSOCIATION AND VERY HIGH RELATIVE RISKS
08 TO HELP US HERE.
09 DOSE RESPONSE IS PERTINENT IN THAT WE WOULD
10 EXPECT TO FIND DOSE-RESPONSE RELATIONSHIPS, BUT AGAIN, IF
11 ONE'S LOOKING EVEN AT THE HIGHER DOSES KNOWN, RELATIVELY
12 LOW RELATIVE RISKS THAT MAY BE DIFFICULT TO QUANTIFY
13 BECAUSE THE IMPLICATION IS THAT WE CAN DETERMINE RELATIVE
14 RISKS THAT EVEN LOWER EXPOSURES THAN THE HIGH ONES THAT
15 HAVE LOW RELATIVES RISKS. SO THAT MIGHT BE DIFFICULT.
16 TEMPORALITY IS IMPORTANT, ALTHOUGH I WOULD
17 SAY THAT I DON'T HAVE THE SAME CONCERN ABOUT LATENCY
18 HERE.
19 MOST OF US ARE -- WE'RE EITHER SMOKERS OR
20 PASSIVE SMOKERS, AND IN FACT THE CARCINOGENS AND THE
21 ACTIONS ARE SOMEWHAT SIMILAR TO CIGARETTE SMOKING, YOU
22 ONLY NEED A LATE EFFECT OF DIESEL. AND SINCE WITH
23 CIGARETTE SMOKING WITHIN FIVE YEARS OF STOPPING YOU GET
24 REDUCED RISKS, I WOULD BE QUITE CONTENT SAYING THAT THOSE
25 EVIDENCE JUST FOR TEN YEARS FROM FIRST EXPOSURE.

0098

01 BUT THAT'S A ISSUE THAT RELIES ON THE FACT
02 THAT THE MAJORITY OF THESE WORKERS AND THESE COHORTS
03 ACTUALLY DID SMOKE, AND OTHERS THAT THEY DIDN'T WERE
04 EXPOSED TO PASSIVE SMOKING. SO IT MAY HAVE HAD THE EARLY
05 STAGES OF LUNG CANCER DEVELOPMENT ANYWAY PRESENT.

06 YOU DON'T HAVE TO HAVE THEN A TOTAL LONG
07 LATENCY PICTURE FOR AN INDIVIDUAL SOURCE OF LUNG
08 CARCINOGENIC AGENTS LIKE DIESEL EXHAUST.

09 AND FINALLY, I WANT TO TALK A LITTLE BIT
10 ABOUT PLAUSIBILITY. THE -- A LOT OF WHAT I'M SAYING IS IN
11 A PAPER THAT COME OUT THAT WE PUBLISHED IN THE JOURNAL OF
12 EPIDEMIOLOGY. IT CAME OUT EARLIER THIS YEAR, A
13 META-ANALYSIS OF DIESEL EXHAUST EXPOSURE AND LUNG CANCER.

14 AND IN META-ANALYSIS WE TRY TO PULL TOGETHER
15 INFORMATION TO HELP US WITH CAUSAL INFERENCE. I BELIEVE
16 THAT'S THE MAIN FUNCTION OF IT. I DON'T THINK IT ANSWERS
17 THE CAUSAL QUESTIONS, BUT IT CAN HELP US WITH CAUSAL
18 INFERENCE WITH REGARD TO THE POINTS THAT I RAISED EARLIER.

19 WE IDENTIFIED 29 PUBLISHED COHORT AND CASE
20 CONTROL STUDIES. 23 MET THE INCLUSION CRITERIA THAT WE
21 HAVE IN THIS PAPER.

22 CERTAIN STUDIES WERE EXCLUDED, THE COAL AND
23 METAL MINERS BECAUSE OF POTENTIAL ROLE OF MULTIPLE
24 OCCUPATIONAL CARCINOGENS. THIS IS ESPECIALLY RADON. ALL
25 MINERS VIRTUALLY HAVE SOME EXPOSURE TO RADON, AND SO WE

0099

01 JUST LEFT SOME OF THOSE STUDIES OUT.

02 AND STUDIES WITH INADEQUATE LATENCY WHICH WE
03 DEFINED FOR PURPOSES OF THIS POOLING IS LESS THAN TEN
04 YEARS FROM FIRST EXPOSURE, AND THEN STUDIES IN WHICH WORK
05 WITH DIESEL EQUIPMENT OR ENGINES COULD NOT BE CONFIRMED OR
06 RELIABLY INFERRED.

07 NOW, THE DETAILS ARE IN THE PUBLICATION, BUT
08 THE BOTTOM LINE OF THE FIRST PART, OUR FINDINGS DUE TO
09 CHANCE, THE POOLED RELATIVE RISK ESTIMATE WAS 1.33, WITH
10 VERY NARROW CONFIDENCE INTERVALS OF 1.27 TO 1.4.

11 AND ALSO IT WAS NOTEWORTHY THAT 21 OUT OF 23
12 STUDIES HAD RISK ESTIMATES GREATER THAN 1. THE LIKELIHOOD
13 OF THAT BEING DUE TO CHANCE OR THESE FINDINGS HERE BEING
14 DUE TO CHANCE ARE WELL UNDER 1 IN 1,000, DEPENDING ON
15 WHICH SPECIFIC WAY YOU WANT TO LOOK AT IT, BUT IT'S WAY
16 UNDER THAT.

17 SO I WOULD SAY THE LIKELIHOOD OF THESE
18 STUDIES ARE PRODUCING CHANCE FINDINGS, JUST FLUCTUATIONS
19 FROM CHANCE, WE'VE GOT A BIT OF A BLIP THERE, CAN BE RULED
20 OUT AS IMPLAUSIBLE EXPLANATION.

21 NOW, IF WE THEN SAY CHANCE IS NOT A
22 POSSIBILITY, THE SECOND AREA IS BIAS THAT WE WANT TO LOOK
23 AT.

24 THE MAIN ISSUE ABOUT BIAS THAT HAS BEEN
25 RAISED ON THESE STUDIES IS CONFOUNDING BIAS DUE TO

0100

01 SMOKING; HOWEVER, THE POOLED RELATIVE RISK ESTIMATES FOR
02 SMOKING ADJUSTED STUDIES AND UNADJUSTED STUDIES WERE VERY
03 SIMILAR, AS I'LL SHOW IN A MOMENT.

04 SECONDLY, THOSE STUDIES GIVING BOTH SMOKING

05 ADJUSTED AND UNADJUSTED RISK ESTIMATES THERE'S ONLY A
06 SMALL REDUCTION IN THE POOLED RELATIVE RISK IN THOSE
07 STUDIES WHEN THEY WERE ADJUSTED FOR SMOKING.
08 AND THIRDLY, THE RELATIVE RISK ESTIMATE WAS
09 ACTUALLY HIGHER THAN THE OVERALL WAS 1.43 IN STUDIES WITH
10 INTERNAL COMPARISONS. THESE WERE STUDIES WHERE WITHIN THE
11 WORK POPULATION, WORKERS ARE BEING COMPARED WITH WORKERS,
12 AND WHERE IT'S LESS LIKELY THAT CONFOUNDING DUE TO SMOKING
13 COULD RESULT.
14 THIS HERE IF WE LOOK AT THE SMOKING ADJUSTED
15 STUDIES, THE POOLED ESTIMATE WAS 1.35 AND THOSE STUDIES
16 NOT ADJUSTED FOR SMOKING IT WAS 1.33. VIRTUALLY NO
17 DIFFERENCE.
18 NOW, THERE WAS FEWER STUDIES THAT GAVE WHAT I
19 LIKE TO SEE, AND THAT'S WHAT HAPPENS BEFORE AND AFTER YOU
20 ADJUST FOR SMOKING, AND THEY DO GIVE A MIXED PICTURE.
21 THERE ARE ONLY FOUR OF THE -- RATHER, FIVE THAT HAVE THE
22 INFORMATION, AND THEY SURE JUMP AROUND. THIS ONE HAS
23 STAYED ABOUT THE SAME AFTER ADJUSTING FOR SMOKING, AND
24 THIS ONE IN EFFECT DISAPPEARED. THIS ONE IT REDUCED.
25 THIS ONE STAYED ABOUT THE SAME. THIS ONE WENT DOWN FROM
0101
01 ALMOST NO INCREASE, BUT THEY ARE VERY SMALL NUMBERS HERE.
02 NOW, OVERALL WHEN ONE POOLS THIS, THERE IS A
03 SMALL REDUCTION IN THE WEIGHT, AND FROM THAT 1.34 DOWN TO
04 1.26, BUT IT IS NOT, I THINK, SUFFICIENT TO BE WORRIED
05 ABOUT RESIDUAL CONFOUNDING GIVEN ALL THE OTHER INFORMATION
06 THAT I'VE PRESENTED ABOUT SMOKING.
07 THE OTHER ISSUE IS INFORMATION BIAS. THE
08 BIASES WHEN I TALK ABOUT THEM, I ALWAYS JUST DIVIDE THE
09 THREE CONFOUNDING INFORMATION AND SELECTION BIASES THAT BE
10 ONE.
11 IT MAINLY CONCERNS EXPOSURE
12 MISCLASSIFICATION, AND I JUST WANT TO NOTE THAT IN MOST
13 STUDIES, IT WOULD BE NONDIFFERENTIAL BETWEEN THE LUNG
14 CANCER PATIENTS AND OTHERS, THEREFORE REDUCING THE
15 RELATIVE RISK ESTIMATES. NOW, NOT ALL, BUT MANY OF THEM.
16 AND THEREFORE, IT'S NOT, IN MY VIEW, A CRITICAL ISSUE AS
17 FAR AS CAUSAL INFERENCE GOES.
18 THE NEXT ONE IS SELECTION BIAS. AND HERE, IF
19 WE NOTE AGAIN, THE STUDY WITH INTERNAL COMPARISONS HAD
20 HIGHER RISK ESTIMATES, AND THEY ARE LESS LIKELY TO
21 SELECTION BIAS PROBLEMS. THEY ARE COMPARING PEOPLE WITHIN
22 THE SAME COHORT.
23 ANOTHER ONE IS THE HEALTHY-WORKER EFFECT, IN
24 WHICH WE TEND TO UNDERESTIMATE RISK, AND DR. GARSHICK
25 SHOWS A VERY NICE EXAMPLE OF THAT IN HIS OWN WORK.
0102
01 I WOULD NOTE, FOR EXAMPLE, ONE OF THE MAJOR
02 STUDIES BY DR. WONG, ET AL., THE ALL CAUSE S.M.R. FOR ALL
03 DEATHS WAS 0.81, CLEARLY INDICATING A HEALTHY-WORKER
04 EFFECT. AND WHEN YOU ARE LOOKING FOR SMALL RISKS IN WORK
05 PLACE STUDIES, YOU MUST LOOK FOR THE HEALTHY-WORKER
06 EFFECT, AND IF THERE, I BELIEVE YOU MUST ADJUST FOR IT.
07 NOW, WE POOLED THE STUDIES BEFORE ADJUSTING
08 FOR IT, BUT I NOTE THAT IT HAS A MAJOR IMPACT ON SOME OF
09 THESE STUDIES WHEN YOU ADJUST FOR THE HEALTHY-WORKER

10 EFFECT.

11 IN THIS CASE, THE STUDY BY WONG, IF YOU LOOK
12 AT THE DURATION OF EXPOSURE LESS THAN 5 YEARS, 5 TO 9,
13 10 TO 14, THE S.M.R. SHOWS A TREND, BUT ONLY UP TO A
14 RELATIVE RISK ESTIMATE OF 1.07.

15 HOWEVER, SINCE THE OVERALL MORTALITY WAS AT
16 80 PERCENT, IT IS QUITE REASONABLE TO ADJUST THIS
17 ESTIMATE, AND WHEN YOU DO, ADJUST IN A HEALTHY-WORKER
18 EFFECT YOU GET 1.34, WHICH IS EXACTLY WHAT ALL THE OTHER
19 STUDIES ARE FINDING THAT HAVE THINGS LIKE INTERNAL
20 COMPARISONS WHERE YOU DON'T HAVE THAT SAME HEALTHY-WORKER
21 PROBLEM.

22 SO IN THE ARTICLE WE DID LOOK AT -- AND I
23 WANT TO GO THROUGH THEM, BUT THERE ARE ABOUT FOUR STUDIES
24 WHERE WE COULD ADJUST FOR THE HEALTHY-WORKER EFFECT, AND
25 THAT'S ALL PRESENTED THERE.

0103

01 NOW, THE NEXT CRITERION FOR CAUSAL INFERENCE,
02 I WANT TO CONSIDER AS CONSISTENCY ONLY VERY BRIEFLY. 21
03 OF THE 23 STUDIES, AS I MENTIONED BEFORE, HAD RELATIVE
04 RISKS GREATER THAN 1.

05 MORE IMPORTANTLY -- WELL, IN ADDITION. I
06 WOULDN'T SAY MORE IMPORTANTLY, THE TWO STUDIES THAT DIDN'T
07 WERE THE TWO SMALLEST STUDIES.

08 SO IN MY VIEW, THESE STUDIES ARE HIGHLY
09 CONSISTENT. IN FACT, I WAS A LITTLE BIT GOING AT THE
10 META-ANALYSIS ALREADY THINKING ABOUT IT. I EXPECTED TO
11 FIND MORE INCONSISTENCIES THAN WERE ACTUALLY FOUND, AND
12 WITH REGARD TO CONSISTENCY, ALSO IN THE PAPER WE HAVE
13 WHAT'S CALLED A FUNNEL PLOT, WHERE YOU WERE LOOKING TO
14 LOOK AT THE LARGER STUDIES OVER THIS SIDE AND SEE IF THEY
15 HAVE DIFFERENT FINDINGS FROM THE SMALLER STUDIES WITH THE
16 VIEW TO LOOKING AT PUBLICATION BIAS.

17 YOU SEE, THE TWO SMALLER STUDIES HAD NO
18 INCREASE RELATIVE RISKS, BUT ALL THE OTHERS DID. AND ALSO
19 THERE IS NO EVIDENCE FROM THIS FOR PUBLICATION BIAS.

20 AGAIN, IT IS IN THE ARTICLE FOR THOSE OF YOU
21 WHO WANT TO READ MORE ABOUT THAT ISSUE OF PUBLICATION
22 BIAS.

23 NOW, JUST BRIEFLY ON DOSE-RESPONSE, WE WOULD
24 LIKE TO SEE EXPOSURE-RESPONSE RELATIONSHIP. AS
25 DR. GARSHICK POINTED OUT, THERE WERE TWO STUDIES WITH

0104

01 ACTUAL MEASURES, BUT YOU CAN LOOK AT DURATION OF
02 EXPOSURE.

03 SO IT -- EITHER LOOKING AT MEASURES OR THE
04 DURATION, THERE ARE A VARIETY OF STUDIES THAT HAVE SOME
05 INFORMATION THAT RELATES TO DOSE-RESPONSE, AND IN ALL BUT
06 ONE, AND ONLY IN A SUBSET OF ONE, THERE IS A TREND OF
07 INCREASING RISK.

08 HERE YOU SEE .5, .7, 1.8, HERE 11.2, HERE
09 INCREASING -- HERE INCREASING IS DR. GARSHICK'S OWN
10 STUDIES, WHICH I WOULD JUST NOTE THAT IN EPIDEMIOLOGICAL
11 DATA, WHERE YOU'VE GOT MAJOR AGE FACTORS, CALENDAR TIMES,
12 VARIABLES, AND EXPOSURE RELATED TO CALENDAR TIME AND
13 DURATION.

14 IT'S VASTLY DIFFERENT FROM ANALYZING ANIMAL

15 STUDIES, AND YOU CAN'T TAKE MULTI-VARIATE MODELS AND THROW
16 THEM AT DATA LIKE THAT AND EXPECT TO GET ANYTHING OTHER
17 THAN FLIP-FLOPPING OF DOSE-RESPONSE RELATIONSHIPS.

18 SO I PERSONALLY FEEL STILL THAT SOME -- THE
19 INITIAL ANALYSES AND SOME THAT DR. GARSHICK HAS PRESENTED
20 DO SHOW THAT THERE IS A TREND WITHIN THAT COHORT, BUT I
21 JUST WANTED TO YOU TO NOTE THAT YOU CAN LOOK AT ALL THESE
22 OTHER STUDIES AS WELL, AND IN ONLY ONE INSTANCE IN THE
23 REPORTED PEER REVIEW PUBLICATIONS ISN'T THERE EVIDENCE OF
24 SOME TREND WHEN YOU CAN LOOK AT IT EITHER BY DURATION OF
25 EXPOSURE OR -- IN PARTICULAR BY DURATION OF EXPOSURE.

0105

01 I WANT TO TURN TO BIOLOGICAL PLAUSIBILITY AND
02 THE DIESEL EXHAUST HAS BEEN SHOWN TO INDUCE LUNG AND OTHER
03 CANCERS IN THE VARIETY OF ANIMALS.

04 NOW, I FRANKLY DON'T CARE WHETHER THINGS
05 CAUSE TUMORS IN RATS VERY MUCH OR MICE, NOR AM I OVERLY
06 CONCERNED ABOUT THE MECHANISMS, THAT IF THEY DO, I QUITE
07 EXPECT THEY MIGHT BE DIFFERENT, AND I DON'T WANT TO
08 OVEREMPHASIZE THIS, BUT IT JUST HAPPENS IT DOES PRODUCE
09 TUMORS IN THE RATS.

10 SECONDLY, THE DIESEL EXHAUST HAS BEEN SHOWN
11 TO CONTAIN HIGHLY MUTAGENIC SUBSTANCES, INCLUDING P.A.H.'S
12 AND NITRO AROMATIC COMPOUNDS. THESE POINTS ARE TAKEN FROM
13 THE DRAFT DOCUMENT.

14 THIRD, DIESEL EXHAUST CONTAINS MANY
15 SUBSTANCES WHICH OCCUR IN RECOGNIZED COMPLEX MIXTURES OF
16 HUMAN RESPIRATORY CARCINOGENS, INCLUDING CIGARETTE SMOKE
17 AND COAL CARBON EMISSIONS. SO IN MY VIEW, WE CAN DROP THE
18 FIRST ONE IF YOU LIKE, BUT IT IS HIGHLY PLAUSIBLE THAT
19 DIESEL EXHAUST MIGHT CAUSE HUMAN LUNG CANCER.

20 WELL, IF WE LOOK BACK AT THIS LIST THEN,
21 CHANCE CAN BE RULED OUT, BUT NO GOOD BASIS FOR BIAS. THAT
22 IS A SURPRISINGLY CONSISTENT -- WELL, WE ARE LOOKING FOR A
23 WEAK ASSOCIATION, SO WE CAN'T DWELL ON THAT.

24 THERE IS EVIDENCE OF DOSE-RESPONSE, AT LEAST
25 WITH DURATION OF EXPOSURE; TEMPORALITY IS OKAY;

0106

01 PLAUSIBILITY IS OKAY; SO I WOULD ACTUALLY COME OUT WITH
02 STRONGER WORDING. AND I WAS HEARING THE EPIDEMIOLOGY PART
03 OF THE I.A.R.C. COMMITTEE ON DIOXIN EARLIER LAST YEAR AND
04 WENT THROUGH THAT WHOLE PROCESS OF TRYING TO DETERMINE HOW
05 DO WE REACH CONCLUSIONS EPIDEMIOLOGICALLY?

06 AND THE POINT I WOULD MAKE IS ONE CAN SAY,
07 WELL, WE'RE TRYING TO SOME OF US REACH ABSOLUTE SCIENTIFIC
08 CERTAINTY. OTHERS ARE SAYING, WELL, WE WANT TO HAVE
09 ENOUGH INFORMATION TO KNOW IF WE SHOULD REGULATE.

10 AND A LOT OF OUR DISAGREEMENT I THINK IS
11 BECAUSE WE'RE THINKING ON THE DIFFERENT POINTS ON THAT
12 FIELD. AND IF WE SAID, WELL, IS THERE ENOUGH INFORMATION
13 TO SAY THAT WE ALL OUGHT BE PATROLLING THIS SUBSTANCE IN
14 OUR ENVIRONMENTAL, I -- NOT CAUSAL EVIDENCE IN HUMANS,
15 THEN TO ME THE ANSWER IS VERY CLEARLY YES. AND I THINK
16 THAT MOST PEOPLE WHO HAVE CONSIDERED IT WOULD AGREE WITH
17 THAT.

18 THE ONLY ISSUES CAN WE SAY WITH ABSOLUTE
19 SCIENTIFIC CERTAINTY, WELL, THAT'S NOT SO CLEAR.

20 NOW, I WANT TO JUST VERY QUICKLY JUST NOTE
21 PASSIVE SMOKING YOU GET THESE VARIATIONS IN RELATIVE RISK
22 ESTIMATES FROM STUDY TO STUDY, AND IN FACT, THERE ARE A
23 LOT OF STUDIES OUT THERE WITH RELATIVE RISK ESTIMATES.
24 LESS THAN ONE FOR PASSIVE SMOKING, BUT YOU GET A CENTRAL
25 TENDENCY, AND WE'VE NOW CONCLUDED, I THINK, THAT PASSIVE
0107 SMOKING IS A CAUSE OF HUMAN LUNG CANCER IN THE PRESENCE OF
01 VARIATIONS AND FINDINGS.
02
03 TWO SLIDES MORE.
04 I WANT NOW TO SAY, WELL, IF INDEED DIESEL
05 EXHAUST CAUSES HUMAN LUNG CANCER, SHOULD WE BE SPLITTING
06 HAIRS OVER THE MINOR DETAILS OF QUANTITATIVE RISK
07 ASSESSMENT?
08 WELL, I DON'T THINK SO. AND THIS THE REASON.
09 IF WE JUST LOOK VERY BRIEFLY AND SAY THAT THE LIFETIME
10 RISK OF DYING FROM LUNG CANCER IN THE U.S. IS AROUND ABOUT
11 1 IN 20, IT'S A LITTLE LOWER NOW, BUT LET'S SAY AROUND
12 ABOUT 1 IN 20, VERY ROUGHLY.
13 LET'S JUST SAY FOR ROUND NUMBERS THAT THE
14 AVERAGE RELATIVE RISK OF LUNG CANCER FOR WORKERS EXPOSED
15 TO DIESEL EXHAUST IS OF THE ORDER OF 1.5. NOW, THAT'S FOR
16 ROUND NUMBERS. YOU CAN SAY 1.3, I DON'T CARE.
17 THAT IS AN EXCESS RELATIVE RISK OF 0.5.
18 THEREFORE, THE INCREMENTAL RISK FOR A DIESEL EXPOSED
19 WORKER IS APPROXIMATELY 0.5 IN 20, OR 25 IN 1,000. NOW,
20 LOOK AT 1 IN 20 BACKGROUND, EXCESS .5 AND 20, AMOUNTS TO
21 25 IN 1,000.
22 NOW, STUDIES WITH QUANTITATIVE EXPOSURE
23 ESTIMATES HAVE RELATIVE RISK AROUND ABOUT 1.5 AND DEPICTED
24 BY THE RAILROAD STUDIES BUT OTHERS ALSO, AND EXPOSURES
25 WERE -- I'M JUST GOING TO SAY, OF THE ORDER, VERY, VERY
0108
01 ROUGHLY 50 MICROGRAMS PER METER DIESEL EXHAUST.
02 STATE-WIDE AVERAGE ESTIMATES, HEAVILY WEIGHED
03 TOWARDS URBAN AREAS, ARE ABOUT 4 MICROGRAMS PER METERED
04 CUBE, ROUNDBOUT 10 OR MORE LOWER, VERY ROUGHLY.
05 ASSUMING A ROUGHLY LINEAR RELATIONSHIP
06 BETWEEN EXPOSURE AND EXCESS RISK, THIS AIR LEVEL COULD BE
07 RESPONSIBLE FOR AN ADDITIONAL TWO LUNG CANCER DEATHS PER
08 THOUSAND PERSONS EXPOSED.
09 NOW, I FRANKLY DON'T CARE WHETHER IT'S 2 OR 5
10 OR 10 OR .5. FROM A PUBLIC HEALTH STANDPOINT, IT'S IN THE
11 DOMAIN OF AREAS OF RISK, WHICH IF THERE IS NO THRESHOLD,
12 AND IF ONE DOES THE LINEAR EXTRAPOLATION, HOWEVER YOU DO
13 IT, AND HOWEVER YOU REFINED THESE DATA, IF YOU DON'T GET A
14 NUMBER ROUGHLY LIKE THAT OR SOMEWHERE NEAR THAT, THEN I
15 THINK THERE IS SOMETHING WRONG.
16 SO THIS THEN PUTS DIESEL EXHAUST IN THE
17 DOMAIN OF AREAS WHERE IT SEEMS TO ME THAT WE HAVE ENOUGH
18 HUMAN EVIDENCE TO SAY NOT THAT NECESSARILY THAT'S
19 ESTABLISHED WITH ABSOLUTE SCIENTIFIC CERTAINTY. WE CAN
20 NEVER DO THAT, BUT THERE'S ENOUGH EVIDENCE BASED ON HUMAN
21 STUDIES THAT THERE ARE -- IT IS INDEED A CAUSE OF HUMAN
22 LUNG CANCER, AND SIMPLE RISK CALCULATIONS WILL SHOW THAT
23 IT'S IN THE DOMAIN OF THINGS WHERE WE ARE TAKING ACTION TO
24 TRY AND REDUCE HUMAN EXPOSURES.

25 THANK YOU.

0109

01 DR. FROINES: OUR NEXT SPEAKER IS KATHARINE HAMMOND

02 WHO, AS YOU HEARD, WORKED IN THE PAST WITH TOM SMITH WHEN

03 THEY WERE IN BOSTON WOESTER AREA, AND KATHIE IS NOW

04 ASSOCIATE PROFESSOR OF INDUSTRIAL HYGIENE AT UNIVERSITY OF

05 CALIFORNIA BERKLEY.

06 I THINK IT'S VERY IMPORTANT TO HAVE PEOPLE

07 LIKE R.C. YU, WHO WORKS FOR ME, AND KATHIE AND TOM SMITH

08 COMMENT ABOUT THESE ISSUES BECAUSE MOST OF THE STUDIES WE

09 DO ARE OCCUPATIONAL EPIDEMIOLOGIC STUDIES AS OPPOSED TO

10 ENVIRONMENTAL STUDIES. AND SO IT'S GOOD TO HAVE PEOPLE

11 PROVIDING TESTIMONY WHO -- WHO REALLY DO UNDERSTAND THE

12 DIFFICULTIES IN OCCUPATIONAL EXPOSURE ESTIMATION, AND

13 THOSE DIFFICULTIES ALWAYS EXIST, AND IT ALWAYS MAKES

14 DEFINING THE PERFECT OCCUPATIONAL EXPOSURE MORE DIFFICULT.

15 AND SO I THINK IN -- IN TALKING ABOUT THIS,

16 WE NEED TO LEARN WHAT ARE SOME OF THE LIMITS BECAUSE I

17 THINK THAT SOMETIMES THOSE LIMITS BECOME USED FOR TRYING

18 TO PARALYZE A PROCESS WHICH ACTUALLY NEEDS TO BE MOVED

19 FORWARD.

20 DR. HAMMOND: THANK YOU, JOHN. I'M NOT GOING TO

21 PRESENT THE PERFECT EXPOSURE ASSESSMENT. ALL RIGHT?

22 DISCLAIMER.

23 LET'S SEE. MAY I HAVE THE SLIDES, PLEASE.

24 OKAY. I'M -- WAS ONE OF THE CO-INVESTIGATORS

25 ALSO IN THE DIESEL EXHAUST STUDY THAT ERIC GARSHICK SPOKE

0110

01 ABOUT AND TOM SMITH. AND I'M GOING TO TALK SOME ABOUT HOW

02 WE CAN INTERPRET SOME DATA FROM THAT ESPECIALLY

03 HISTORICALLY, AND ALSO SOME OTHER OCCUPATIONAL EXPOSURES

04 TO DIESEL EXHAUST. AND THIS IS REALLY IN THE REALM OF

05 WITHOUT HAVING PERFECT EXPOSURE ASSESSMENT, WHAT CAN WE

06 SEE AND WHEN CAN WE KNOW.

07 FIRST OF ALL, SO THIS IS THE STUDY -- THE

08 FIRST PART OF MY TALK WILL BE THE RAILROAD EXPOSURES, AND

09 THEN WE'LL TALK ABOUT OTHER EXPOSURES.

10 WE DID SAMPLE, WE COLLECTED OVER 500 PERSONAL

11 SAMPLES, ALMOST 300 AMONG TRAIN CREW AT FOUR RAILROADS,

12 JUST TO GIVE YOU A SENSE THAT THIS IS A LOT OF DATA THAT'S

13 COLLECTED WITH ITS OWN LIMITATIONS.

14 AND THESE WERE COLLECTED AS A SET OF FOUR

15 RAILROADS IN 1982 TO 1983. ONE OF THE QUESTIONS HAS BEEN,

16 WHAT DOES THIS -- THIS DATA COLLECTED IN 1982-'83 TELL US

17 ABOUT EXPOSURE IN ANY OTHER TIME PERIOD.

18 AND SO I THINK, FIRST, LET'S GO BACK AND

19 THINK ABOUT WHAT DO WE -- HOW DO WE THINK ABOUT DIESEL

20 EXHAUST EXPOSURE HISTORICALLY AMONG RAILROAD WORKERS AND

21 THIS IS NOT MY ORIGINAL IDEA, OF COURSE. THIS IS COMING

22 FROM THE DOCUMENT. BUT THE ROOF MODEL THAT TAKES -- SHOW

23 AN INCREASE FROM 1945 TO 1959, AND THEN A DECREASE, I

24 THINK, IS THE MOST APPROPRIATE MODEL TO LOOK AT THIS.

25 THIS IS NOT TO ANY SCALE, BUT THE CONCEPT

0111

01 HERE IS THAT FROM '45 TO '59, WE AT LEAST THINK THAT THE

02 EMISSIONS FROM THE TRAINS MAY NOT HAVE CHANGED. THE

03 REASON THE AVERAGE WORKER'S EXPOSURE INCREASED IS THAT

04 THAT THE PERCENT OF WORKERS EXPOSED INCREASES. SO THE
05 OCCUPATIONAL AVERAGE WOULD BE INCREASING IN ANY CATEGORY.
06 BY '59 THERE WAS 95 PERCENT DIESELIZATION.

07 NOW, FROM 1959 TO 1980 THERE'S HAS -- THERE
08 HAS BEEN A LOT OF CONJECTURE ABOUT A DECREASE IN
09 EXPOSURES, AND I'VE HEARD FACTORS OF TEN OR EVEN HIGHER
10 SUGGESTED IN THE -- WHAT WOULD BE THE RATIO FROM THIS PEAK
11 DOWN TO THE 1980 EXPOSURES, AND THE SUGGESTION THAT SINCE
12 OUR MEASURED VALUES WERE MADE IN 1980, IT MEANS THAT IN
13 PAST, THE LEVELS WERE TEN TIMES HIGHER. AND I WANT TO
14 TELL YOU WHY I THINK THAT MAYBE IS AN ERRONEOUS
15 INTERPRETATION OF SOME OF THIS DATA.

16 FIRST, LET'S LOOK AT WHAT'S THE DATA WE DID
17 COLLECT, AND WHAT DO WE NO ABOUT IT.

18 THIS -- THIS IS LOOKING AT THE AGE OF THE
19 LOCOMOTIVES AT THE FOUR RAILROADS WHICH WERE STUDIED. AND
20 AS YOU WILL SEE, ALL FOUR RAILROADS WERE -- HAD OVER HALF
21 OF THEIR LOCOMOTIVES WERE FIRST GENERATION DIESEL.

22 OKAY. SO WE'RE NOT TALKING ABOUT HAVING THE
23 LATEST GENERATION CARS. THESE ACTUALLY ARE SMALL
24 RAILROADS. THEY GET THE HAND ME DOWNS; RIGHT? AND ONLY A
25 VERY SMALL PERCENTAGE OF THE DIESELS WERE MADE AFTER 1970.

0112

01 AND IN FACT, TWO OF THE RAILROADS -- ALTHOUGH
02 ALL OF THE RAILROADS HAD OVER 50 PERCENT OF THEIR CARS
03 MADE IN THE FIRST GENERATION OF THEIR LOCOMOTIVES, TWO
04 WERE AROUND 55 PERCENT AND TWO WERE OVER 80 PERCENT, FIRST
05 GENERATION DIESEL.

06 NOW, WHEN THE RAILROADS ARE NUMBERED ONE,
07 TWO, THREE, FOUR, AND THIS ORDER WILL BE MAINTAINED
08 THROUGHOUT MY PRESENTATION, EVEN THOUGH IT MIGHT BE NICER
09 TO GROUP THEM, BUT THAT'S THE STANDARD ORDER WE'VE USED.

10 SO I WOULD LIKE TO JUST QUOTE DIRECTLY FROM
11 SUSAN WOSKIE'S COMMENTS ABOUT OUR DATA. THIS IS FROM HER
12 PAPER. AFTER THE INITIAL DIESELIZATION OCCURRED IN THE
13 EARLY 1950'S, A SECOND GENERATION OF MORE EFFICIENT DIESEL
14 LOCOMOTIVES WAS INTRODUCED INTO THE LARGER COMPANIES
15 DURING THE '60'S.

16 THERE WERE ANECDOTAL REPORTS THE OLDER FIRST
17 GENERATION LOCOMOTIVES WERE SMOKIER THAN THE SECOND
18 GENERATION, A CHANGE WHICH MAY HAVE DECREASED DIESEL
19 EXPOSURES TO THE TRAIN CREW OVER TIME.

20 NOW, I HAVE ADDED THESE ITALICS. MOST OF THE
21 LOCOMOTIVES OF THE ROSTERS OF THE SMALL RAILROADS WE
22 SAMPLED WERE FIRST-GENERATION BUILT BEFORE 1960. MANY OF
23 THE LARGER U.S. RAILROADS MAY HAVE MORE MODERN SECOND
24 GENERATION DIESELS.

25 AND THEN THIS LEADS TO THE CONCLUSION, IT'S

0113

01 ASSUMED THAT THE NATIONAL CAREER GROUP EXPOSURES FOR THE
02 BREAKER, CONDUCTOR, AND ENGINEER FIRER GROUPS REPRESENT
03 THE NATIONAL AVERAGE LEVEL AND VARIABILITY OF EXPOSURE
04 THAT OCCURRED DURING THE PERIOD OF THE EPIDEMIOLOGIC
05 STUDIES.

06 NOW, LET'S SEE IF I CAN DO A REVERSE HERE.
07 LET ME GO BACK HERE NOW TO THE -- THIS SLOPE.

08 IN OTHER WORDS, WHAT WE'RE SAYING IS THAT

09 ALTHOUGH THE SAMPLES WERE COLLECTED DURING THIS TIME, THEY
10 DON'T REPRESENT THE NATIONAL AVERAGE DURING THAT TIME,
11 1980, BUT RATHER PROBABLY THEY REPRESENT EXPOSURES UP
12 DURING -- NEARER TO THE PEAK OF THIS ROOF. BECAUSE OVER
13 HALF THE CARS WERE PRODUCED BEFORE THAT TIME, TO THE
14 DEGREE THERE'S ANY DIFFERENCE IN EMISSIONS IN THE CARS.
15 I'M GOING THE WRONG WAY. SORRY.
16 NOW, I DID DO A LITTLE LOOKING AT RAILROAD
17 ONE. WE ACTUALLY HAD THE INFORMATION FOR THE AGE OF THE
18 RAILROADS BY THE LOCOMOTIVES, BY WHICH TASK THEY WERE USED
19 FOR, AND COULD SAY FOR EACH OF THESE JOB GROUPS WHAT
20 PERCENTAGE OF FIRST GENERATION DIESELS, THESE SMOKIER
21 DIESELS THEY HAD.
22 AND YOU WILL NOTICE THAT, FOR INSTANCE, AMONG
23 THE ENGINEER FIRERS, WE SEE THAT THE FREIGHT PEOPLE HAD --
24 THEY HAD THE NEW CARS, OKAY. THE PASSENGERS IN THE YARD
25 HAD THE OLD CARS. AND YOU KNOW, STAN MAY TRY TO TELL ME
0114
01 THAT THERE'S SOME DIFFERENCE HERE. I'M NOT CLEAR. I
02 THINK, YOU KNOW, THERE MAY BE SOME DIFFERENCE BETWEEN
03 THIS, BUT THERE'S NOT A HUGE DIFFERENT. THERE'S NO MORE
04 THAN A FACTOR OF TWO DIFFERENCE BETWEEN THOSE THAT HAVE
05 THE FIRST GENERATION.
06 IN FACT, WHICH WAY DOES IT GO? THE FIRST
07 GENERATION, THOSE THAT HAVE MOST FIRST GENERATION DIESEL
08 HAVE LOWER EXPOSURES.
09 SIMILARLY, IF WE LOOK AT THE BREAKER
10 CONDUCTOR GROUP, WHAT WE FIND IS THE NEWER -- THOSE PEOPLE
11 WHO ARE WORKING THE NEWER ENGINES ACTUALLY DON'T HAVE ANY
12 SIGNIFICANTLY LOWER EXPOSURE. IN FACT, IT MAY BE SLIGHTLY
13 HIGHER, BUT I DON'T WANT TO MAKE A POINT OF THAT.
14 THE REAL POINT HERE IS WE'RE NOT SEEING ANY
15 MAJOR DIFFERENCE BETWEEN ANY EXPOSURES BETWEEN THESE.
16 SIMILARLY, I LOOKED AT THE NITROGEN DIOXIDE
17 BY ALL THE DIFFERENT RAILROADS, AND -- OH, SORRY ABOUT
18 THIS LAST COLUMN MISSING. BUT THE -- RECALL THAT
19 RAILROADS ONE AND FOUR HAVE MORE OF THE NEWER TRAINS THAN
20 RAILROADS TWO AND THREE, AND AGAIN, WITH A COUPLE OF
21 EXCEPTIONS, THERE'S NOT REALLY A HUGE DIFFERENCE IN THE
22 EXPOSURES TO NITROGEN DIOXIDE.
23 THE SAME IS TRUE FOR PARTICLES, BUT I
24 WASN'T -- THIS SLIDE GOT LOST. I'LL SHOW YOU IN JUST A
25 SECOND.
0115
01 SO OKAY. NOW, I WANT YOU TO LOOK HARD AT
02 THIS. THIS IS A LOCOMOTIVE; RIGHT? IT'S NOT TO BE
03 CONFUSED WITH YOUR COMPUTER. YOU MAY NOT HAVE GOTTEN
04 CONFUSED BY IT, BUT LET ME -- YOU THINK ABOUT THE FACT
05 THAT EVERYONE SAYS P.C.'S ARE OBSOLETE AFTER THREE YEARS.
06 NOW, MAYBE YOU WOULD SAY FIVE, WHATEVER, THAT WE TURN
07 THESE OVER.
08 RAILROAD LOCOMOTIVES DON'T GET OBSOLETE THAT
09 QUICKLY, AND THERE'S AN UNDERLYING ASSUMPTION THAT IN
10 1980, MOST RAILROAD COMPANIES HAD CARS THAT WERE PRODUCED
11 IN THE LAST FIVE YEARS, AND THAT'S NOT AT ALL TRUE.
12 WHEN WE LOOKED AT THREE MAJOR RAILROADS IN
13 THE COUNTY AND WHAT THEIR ROLLING STOCK LOOKED LIKE DURING

14 THE TIME OF OUR STUDY IN 1982-'83, AND THE TIME IT WOULD
15 BE RELEVANT TO THE EPISTUDY, YOU'LL NOTICE THAT THEY WERE
16 STILL USING -- TWO OF THE THREE RAILROADS STILL HAD
17 SIGNIFICANT AMOUNT OF STOCK IN FIRST GENERATION DIESEL,
18 BETWEEN 25 AND 60 SOME PERCENT.

19 SO THEY DON'T THROW THEM OUT. THERE'RE NOT
20 THE, YOU KNOW, 286'S. THEY ARE NOT MY FATHER'S
21 OLDSMOBILE.

22 NOW, IF WE COMPARE THE AGE OF THE LOCOMOTIVES
23 IN THE RAILROAD WORKERS' EPIDEMIOLOGIC STUDY WHERE HE DID
24 THE SAMPLING WITH THOSE OF THESE THREE MAJOR RAILROADS, WE
25 WILL DEFINITELY SEE THAT IN THIS -- WHERE THE SAMPLING WAS
0116

01 CONDUCTED, WE DID HAVE A HIGHER PROPORTION OF FIRST
02 GENERATION DIESEL COMPARED WITH THE THREE MAJOR
03 RAILROADS.

04 SO DEFINITELY WE WERE LOOKING AT OLDER
05 RAILROADS, BUT EVEN THE MORE -- THE NEW, LARGE RAILROADS
06 ALSO HAD VERY SIGNIFICANT NUMBERS OF THE FIRST GENERATION
07 DIESELS.

08 OKAY. SO -- SO THAT WAS MY FIRST POINT.

09 THE SECOND ONE IS TO SAY QUICKLY ABOUT
10 BACKGROUND CORRECTION. THERE'S BEEN A LOT OF DISCUSSION
11 ON HOW TO CORRECT FOR BACKGROUND. AND I WOULD SAY THAT
12 BASICALLY THERE ARE THREE MAJOR OPTIONS: ONE IS TO DO
13 NOTHING TO CORRECT FOR BACKGROUND; ONE IS TO SUBTRACT THE
14 CLERKS' LEVEL SINCE THE CLERKS ARE ASSUMED TO HAVE NO
15 DIESEL EXPOSURE; AND ONE IS TO SUBTRACT AMBIENT AIR
16 CONCENTRATIONS WHICH WOULD BE APPROXIMATELY 10 TO 20
17 MICROGRAMS PER CUBIC METER RESPIRABLE.

18 AND I WOULD SUGGEST THE LATTER IS REALLY THE
19 BEST WAY. THE CLERKS ARE PROBABLY EXPOSED TO OTHER
20 MATERIAL THAN DIESEL JUST AS PEOPLE IN -- INDOOR AIR WILL
21 HAVE HIGHER EXPOSURES ON A FIXED SAMPLER INDOORS.

22 BUT I THINK THAT, IN FACT, THE -- IT'S AN
23 OVERCORRECTION TO TAKE WHATEVER THE CLERKS' EXPOSURES ARE
24 AND SUBTRACT THEM. THAT'S NOT THE AMBIENT LEVEL IN THOSE
25 AREAS.

0117

01 OKAY. LET ME NOW TURN TO A FEW OTHER
02 OCCUPATIONS FOR WHICH THE META-ANALYSIS WAS DONE, AND AN
03 EXAMINATION OF WHAT THEIR EXPOSURES ARE. SO I'M GOING TO
04 BE TALKING ABOUT BUS GARAGE WORKERS, MECHANICS, HEAVY
05 EQUIPMENT OPERATORS, AND DRIVERS.

06 AND TO START THIS, I HAVE TO EXPLAIN, AGAIN,
07 THE DIFFICULTY WE HAVE THAT DIESEL EXHAUST IS NOT A SIMPLE
08 MATERIAL. IT'S NOT LOOKING AT PHENANTHRENE OR BENZENE OR
09 ASBESTOS, AND HAVE TO -- AND WE'RE LOOKING AT THIS MIXTURE
10 AND WE HAVE SURROGATES RATHER THAN A STRAIGHT FORWARD
11 THING.

12 NOW, ONE SURROGATE -- ONE WAY TO THINK ABOUT
13 THIS IS WE LOOK AT RESPIRABLE PARTICLES BY THEMSELVES.
14 RESPIRABLE PARTICLES CAN BE THOUGHT OF AS -- ALL, AS BEING
15 COMPOSED OF DIESEL, RESPIRABLE PARTICLES FROM
16 ENVIRONMENTAL TOBACCO SMOKE, FROM OTHER SOURCES INDOORS,
17 AND THEN FROM WHATEVER BACKGROUND IS THERE. NOT INDOORS,
18 JUST OTHER SOURCES THAT MAY BE IDENTIFIED IN A PARTICULAR

19 LOCATION.
20 WE USE THE TERM ADJUSTED RESPIRABLE PARTICLES
21 IN OUR STUDIES TO REFER TO WHERE WE HAVE AT LEAST BEEN
22 ABLE TO SUBTRACT OUT THE ENVIRONMENTAL TOBACCO SMOKE
23 COMPONENT OF THAT, SO THAT OURS INCLUDES DIESEL -- BUT IT
24 ALSO INCLUDES WHAT OTHER SOURCES MIGHT BE THERE AND
25 BACKGROUND.

0118
01 ANOTHER THING THAT IS USED IS AN ELEMENTAL
02 CARBON HAS BEEN USED IN A LOT OF STUDIES AS A SURROGATE
03 FOR DIESEL. THERE'S ALSO AN ORGANIC CARBON, AND IF YOU
04 WERE TO TAKE A SAMPLE THAT WAS JUST DIESEL EXHAUST, THE
05 RESPIRABLE PARTICLES WOULD BE COMPOSED OF ELEMENTAL AND
06 ORGANIC CARBON PREDOMINANTLY.

07 HOWEVER, IN THE NATURAL ENVIRONMENT, THERE
08 ARE LOTS OF SOURCES OF ORGANIC CARBONS SO OFTEN -- AND
09 THERE'S NOT SO MANY FOR ELEMENTAL CARBONS. SO ELEMENTAL
10 CARBON IS A MORE SPECIFIC MARKER FOR DIESEL EXHAUST, AND
11 THEN WE JUST NEED TO FIND A WAY TO COMPARE TO CHANGE THIS
12 VALUE TO RESPIRABLE FROM DIESEL.

13 WHAT I'M TRYING -- TRIED TO DO IN THE
14 FOLLOWING ANALYSES IS TO CONVERT EVERYTHING TO RESPIRABLE
15 PARTICLES FROM DIESEL. AND FOR ELEMENTAL CARBON, I HAVE
16 VERY SIMPLY MULTIPLIED THAT VALUE BY TWO BASED ON MY
17 EXAMINATION OF THE DATA, WHICH WE CAN TALK ABOUT ANOTHER
18 TIME IF YOU WANT. BUT ASSUME THAT 50 PERCENT OF DIESEL
19 EXHAUST WAS ELEMENTAL CARBON. SO IF WE MULTIPLIED BY TWO,
20 WE WOULD HAVE AN ESTIMATE OF THE RESPIRABLE FROM DIESEL.

21 SO LET'S TURN TO BUS DRIVERS, AND ONE STUDY
22 THAT IS VERY INTERESTING -- ACTUALLY, IT'S A PAIR OF
23 STUDIES THAT WERE DONE, LOOKING AT EXPOSURES IN 1959 AND
24 1979, 20 YEARS LATER, IN SOME LONDON BUS DRIVERS -- AND
25 ACTUALLY THEY USED ANOTHER SURROGATE. IT'S REFLECTANCE.

0119
01 AND FOR THESE PURPOSES AS I LOOKED AT THE DATA AND
02 COMPARED DATA OF TOTAL SAMPLES WITH REFLECTANCE, I DECIDED
03 THEY WERE ALL -- ALMOST ALWAYS LESS THAN THE TOTAL
04 PARTICLES. AND SO I DECIDED JUST SAY REFLECTANCE WAS
05 APPROXIMATELY EQUAL TO THE RESPIRABLES FROM DIESEL. THAT
06 IS THE CURRENT ASSUMPTION.

07 AND THESE WERE ALL CORRECTED FOR VALUES THAT
08 WERE TAKEN ON THE ROOF OF THE GARAGE TO CORRECT FOR
09 AMBIENT SOURCES OF REFLECTANCE.

10 ONE VERY INTERESTING THING IS THEY SAW NO
11 SIGNIFICANT CHANGE IN THESE -- THEY WERE AT TWO DIFFERENT
12 GARAGES OVER THIS 20-YEAR PERIOD, IF NO NEW BUSES CAME IN.
13 THERE WAS NOT A HUGE DIFFERENCE.

14 NOW, THESE WERE AREA SAMPLES, NOT PERSONAL
15 SAMPLES, AND THEY WERE PLACED GENERALLY WITHIN THE AREAS
16 WHERE THE HIGHEST LEVELS -- THE HIGHEST CONCENTRATIONS
17 WERE EXPECTED.

18 WHAT I DID WITH THAT DATA IS I MADE -- I
19 CALCULATED A TIME WEIGHT AVERAGE OF THE CONCENTRATION
20 DURING THE TIME THE BUSES WERE RUNNING, WHICH WAS ABOUT
21 FOR 20 HOURS, FIGURING THAT WAS WHEN PEOPLE WERE THERE.
22 AND NOW KNOWING THESE ARE AT THE HIGHEST AREAS, AND THAT
23 THEY ARE AREA SAMPLES, I MADE THE ASSUMPTION FROM WHAT I

24 FOLLOW THROUGH HERE THAT THE MAXIMUM AVERAGE PERSONAL
25 EXPOSURE WOULD BE HALF OF THAT. YOU KNOW, MAYBE IT WOULD
0120
01 BE LESS, BUT PROBABLY THAT'S A HIGH ESTIMATE OF THE
02 PERSONAL EXPOSURE BECAUSE THESE WERE AT FIXED LOCATIONS
03 WITH HIGH LEVELS.
04 USING THAT AND GOING THROUGH ALL THE DATA,
05 THEN THE ESTIMATE IS WITH THE RESPIRABLE PARTICLES FROM
06 DIESEL WERE -- AT ONE RAILROAD -- AT ONE GARAGE IT WAS 80,
07 AND THE OTHER IT WAS 300. SO THOSE ARE TWO ESTIMATES AT
08 TWO DIFFERENT LOCATIONS.
09 OKAY. SO THAT BECOMES ONE -- PIECE OF DATA
10 FOR BUS GARAGES. GAMBLE LOOKED AT FOUR GARAGES THAT HAD
11 RESPIRABLES PARTICLES. THESE WERE THE AVERAGE
12 CONCENTRATIONS IN EACH OF THOSE, BUT THOSE INCLUDED
13 SMOKERS. IF YOU TOOK THE AVERAGE OF ALL THE NONSMOKERS,
14 THE AVERAGE WAS 230 MICROGRAMS PER CUBIC METER, AND THAT'S
15 RESPIRABLE PARTICLES, BUT THERE'S NOT ENVIRONMENTAL
16 TOBACCO SMOKE, HOPEFULLY OR LESS.
17 BIRCH AND CARY DID ELEMENTAL CARBON, WHICH IS
18 MORE SPECIFIC, AND YOU DON'T GET A CONTRIBUTION FROM
19 TOBACCO SMOKE FROM THAT, AND THEY GOT AN ELEMENTAL CARBON
20 LEVEL OF 98 MICROGRAMS PER CUBIC METER, AN ORGANIC OF 80.
21 ORDINARILY, I WOULD MULTIPLY THIS BY TWO, BUT SINCE THE
22 ACTUAL LEVEL WAS LESS THAN TWICE THAT, I JUST TOOK THE
23 ADDITION. SO IT'S 180.
24 SO IF YOU LOOK AT THESE VALUES 80, 300, 230,
25 180, BASICALLY, I SAID MY BEST ESTIMATE IS THAT ON
0121
01 AVERAGE, THE LEVELS ARE SOMEWHERE BETWEEN 50 AND 200
02 MICROGRAMS PER CUBIC METER, WITH A MAXIMUM ESTIMATE THERE
03 AT 500.
04 OKAY. TURNING TO HEAVY EQUIPMENT OPERATORS.
05 DOUG FOWLER DID SOME WORK IN THE EARLY '80'S WHERE HE WAS
06 LOOKING AT PEOPLE WHO -- MEMBERS OF THE LOCAL UNION IN
07 CALIFORNIA, AND HE TOOK PERSONAL SAMPLES ON -- I THINK A
08 COUPLE HUNDRED PEOPLE. AND AGAIN, THEY USED ELEMENTAL
09 CARBON AS THE SURROGATE. THE AVERAGE CONCENTRATION WAS
10 3.2 MICROGRAMS PER CUBIC METER, WHICH IF WE USE THE FACTOR
11 OF 2, GIVES US A RESPIRABLE FROM DIESEL OF ABOUT 6.4.
12 NOW, I THINK IT'S IMPORTANT AS WE LOOK AT --
13 THAT MAY BE THE AVERAGE EXPOSURE DURING THE TIME THAT ONE
14 IS EXPOSED, BUT IT'S IMPORTANT TO REMEMBER THAT PROBABLY
15 THESE PEOPLE DON'T HAVE THE STANDARD 40-HOUR WEEK,
16 50 WEEK A YEAR, 40 YEARS LIFETIME EXPOSURE THAT MANY OTHER
17 PEOPLE DO. CONSTRUCTION JOBS ARE MUCH MORE SPORADIC, AND
18 I THINK THAT TO REALLY LOOK AT THAT AND TO TRY TO PUT THIS
19 IN SOME PERSPECTIVE WHEN WE ARE REALLY INTERESTED IN THE
20 CUMULATIVE EXPOSURE, ONE WOULD WANT TO GO BACK AND DO A
21 STUDY OF WHAT THE TYPICAL WORKDAY IN A YEAR OF A
22 CONSTRUCTION WORKER IS.
23 BUT I -- I WOULD IMAGINE THAT MEANS THE
24 AVERAGE YEARLY EXPOSURE WOULD BE LESS THAN WHAT IT IS
25 DURING THE TIME OF HIS WORKING.
0122
01 BUT WITHOUT HAVING -- I DID NOT MAKE THAT
02 ADJUSTMENT. SO DURING -- DURING THE TIME THAT THEY ARE

03 WORKING, THE RESPIRABLE IS 5 TO 10 MICROGRAMS PER CUBIC
04 METER WITH A MAXIMUM OF 50.

05 IF YOU LOOK AT TRUCK DRIVERS, DENNIS ZAEPST
06 HAS DONE A MAJORITY OF THE MEASUREMENT WORK THERE. AND
07 AGAIN, THEY USED ELEMENTAL CARBON AS THE SURROGATE. THEY
08 FOUND THAT LOCAL DRIVERS WERE 5.4, AND ROAD 5.1, WHICH
09 TELLS US THE RESPIRABLE FROM DIESEL IS 10 TO 11.

10 DURING THE SAME STUDY THAT I MENTIONED ABOUT
11 HEAVY EQUIPMENT WORKERS, DOUG FOWLER ALSO MEASURED HIGHWAY
12 CONCENTRATIONS ALONG THE HIGHWAY DRIVING IN THE CAR, AND
13 FOUND ELEMENTAL CARBONS OF 7.2, WHICH WOULD INDICATE 14;
14 IF YOU ASSUME THAT MOST OF THE EXPOSURE OF DRIVERS IS FROM
15 JUST BEING ON THE HIGHWAY.

16 SO THIS WOULD LEAD US TO SAY THAT PROBABLY
17 THE RESPIRABLE FROM DIESEL IS 10 TO 15 MICROGRAMS PER
18 CUBIC METER.

19 NOW, AGAIN, THAT'S DURING THE TIME THAT ONE'S
20 DOING THESE THINGS, AND IT'S DURING THIS TIME PERIOD.

21 SOME CAVEATS I WOULD HAVE. FIRST, IT MAY BE
22 THAT DRIVERS MAY HAVE OVER 40 HOURS A WEEK EXPOSURE. NOW,
23 THIS IS NOT BASED ON MY DOING ANY STUDIES. IT'S MY BEING
24 A DRIVER, AND KIND OF WHAT I'VE HEARD ABOUT TRUCK DRIVERS
25 WORKING MANY MORE HOURS THAN 40 HOURS A WEEK AND DOING
0123

01 LONG DRIVES.

02 AND ALSO THEY MAY SLEEP IN THEIR CABS WHICH
03 EITHER -- WITH THEIR ENGINES RUNNING, WHICH MAY PRODUCE
04 SOME EXPOSURE, OR NEAR THE HIGHWAY, WHICH MEANS THEY MAY
05 JUST BE GETTING HIGHWAY EXPOSURE WHILE THEY ARE SLEEPING.
06 SO THEIR EXPOSURES MAY NOT JUST BE FROM WHILE THEY ARE
07 DRIVING.

08 SO AGAIN, I THINK A LITTLE STUDY OF THE FULL
09 DYNAMICS OF WHAT HAPPENS IN THE YEAR OF A TRUCK DRIVER
10 WOULD BE IMPORTANT IN INTERPRETING THIS DATA.

11 ANOTHER IMPORTANT POINT, WHICH DENNIS ZAEPST
12 BRINGS UP THAT THEY HAVEN'T LOOKED AT IS THAT THE OLDER
13 EXHAUST DESIGN -- CURRENTLY, OF COURSE, THE EXHAUST GOES
14 OFF THE TOP OF THE CABIN AND BACK. IT USED TO EXHAUST
15 UNDERNEATH, WHICH MIGHT HAVE LEAD TO MUCH HIGHER
16 EXPOSURES. SO I THINK HISTORICALLY ONE NEEDS TO LOOK AT
17 SOME OF THOSE ISSUES TO UNDERSTAND THAT BETTER.

18 SO WHAT WE HAVE IS WE HAVE CURRENT EXPOSURES.
19 AGAIN, I HAVEN'T DONE AN ADJUSTMENT FOR THOSE. SO JUST TO
20 SUMMARIZE THIS DATA FOR THESE FOUR DIFFERENT OCCUPATIONAL
21 GROUPS, THAT THE RANGE OF BUS GARAGE WORKERS IS ON THE
22 ORDER OF 50 TO 200, WITH A MAXIMUM OF 400 TO 500, AND WE
23 DO HAVE SOME INFORMATION THAT HISTORICALLY, IT WASN'T
24 NECESSARILY HIGHER THAN THAT.

25 MECHANICS BETWEEN 15 AND 150. AND IT'S
0124

01 HIGHLY VARIABLE DEPENDING ON THE GARAGE AND THE DESIGN OF
02 VENTILATION.

03 HEAVY EQUIPMENT OPERATOR 5 TO 10, BUT THESE
04 PEOPLE MAY WORK LESS, SO THEIR CUMULATIVE EXPOSURE MAY BE
05 LESS.

06 TRUCK DRIVERS 10 TO 15. I THINK THEY MAY
07 WORK MORE, AND SO THEIR CUMULATIVE EXPOSURES MAY BE MORE,

08 PLUS I THINK OUR HISTORICAL DATA IS MUCH WEAKER IN THAT.
09 SO I THINK THAT'S IMPORTANT.

10 SO WE ARE PROBABLY -- MY -- MY CONCLUSIONS
11 HERE WOULD BE THAT THESE NUMBERS MAY BE UNDERESTIMATING
12 THE HEAVY EQUIPMENT -- I MEAN, OVERESTIMATING THE HEAVY
13 EQUIPMENT OPERATOR'S EXPOSURES, AND UNDERESTIMATING TRUCK
14 DRIVER EXPOSURES.

15 AND LET ME JUST GO BACK AND SUMMARIZE NOW
16 WHAT WE -- WHAT I SAID ABOUT DIESEL EXHAUST.

17 FIRST OF ALL, I DO THINK THAT THE PROFILE OF
18 THE ROOF IS THE MOST APPROPRIATE TO BE USED.

19 I THINK THE WOSKIE DATA REPRESENTS EXPOSURES
20 TYPICAL OF THE FIRST GENERATION DIESEL LOCOMOTIVES
21 PREDOMINANTLY, ALTHOUGH THERE IS A MIX; THAT THE
22 BACKGROUND CORRECTION IS BEST BY -- IF YOU SUBTRACT THE
23 CLERK ADJUSTED RESPIRABLE PARTICLES, YOU'RE PROBABLY
24 OVERCORRECTING, AND THAT CORRECTION WITH AMBIENT
25 RESPIRABLE PARTICLES IS A BETTER CORRECTION.

0125

01 THAT THE MIX OF LOCOMOTIVES MEANS THAT THE
02 ROOF SLOPE FROM 1959 TO 1980 IS NOT A STEEP ONE. RATHER,
03 I THINK -- I BELIEVE THE RATIO IS ONLY 2 -- 2 OR MAYBE 3.
04 I DOUBT IT'S ANYTHING NEAR 10.

05 AND FINALLY, THAT THE TROOP -- TRUE CREW
06 MEMBER -- TRAIN CREW MEMBERS EXPOSURE, BASED ON THE WOSKIE
07 DATA, IS PROBABLY WHAT WAS AVERAGED 80 MICROGRAMS PER
08 CUBIC METER OF ADJUSTED RESPIRABLE PARTICLES, WHICH MEANS
09 IT'S PROBABLY 60 TO 70 MICROGRAMS PER CUBIC METER. AND I
10 REALLY DON'T THINK THAT GOING BACK OVER TIME WE'RE GOING
11 TO SEE MORE THAN A TWO OR ABSOLUTELY AT MOST A THREE TIMES
12 INCREASED EXPOSURE.

13 SO THE ESTIMATE OF SAYING A MAXIMUM OF 500, I
14 THINK, IS OVERESTIMATING HOW HIGH IT COULD HAVE BEEN IN
15 THE PAST, BUT IT'S CERTAINLY -- I THINK IT'S SAFE. IT'S A
16 SAFE ESTIMATE.

17 OKAY. SO THANK YOU VERY MUCH, AND I THINK
18 IT'S TIME TO END THE DECISION.

19 DR. FROINES: THAT WAS VERY GOOD.

20 CAN WE HAVE SOME LIGHTS?

21 AT THIS POINT, WE WOULD LIKE TO GIVE TOM MACK
22 FROM THE UNIVERSITY OF SOUTHERN CALIFORNIA THE OPPORTUNITY
23 TO COMMENT ON WHAT'S HAPPENED BEFORE HIM, IF HE IS SO
24 INCLINED. I'VE NEVER SEEN HIM NOT SO INCLINED, BUT YOU
25 NEVER KNOW.

0126

01 DR. MACK: THANK YOU. MY CREDENTIALS FOR BEING
02 ASKED TO COME UP AND GIVE COMMENTS BASICALLY COULD BE
03 SUMMARIZED BY SAYING NOBODY HAS EVER GIVEN ME A LOT OF
04 MONEY TO EVALUATE DIESEL EXHAUST, AND THERE'S WHERE I'M
05 RELATIVELY IGNORANT ABOUT THE ISSUE UNTIL THIS MORNING.
06 WELL, THAT'S NOT ENTIRELY TRUE, UNTIL YESTERDAY.

07 I SPENT A FAIR AMOUNT OF TIME WITH THE
08 DOCUMENT AND FIGURED IN THE BEGINNING THAT I KNEW VERY
09 LITTLE, AND I ACCUMULATED A LOT OF PIECES OF PAPERS WITH
10 SOME ERUDITE COMMENTS ABOUT VIRTUALLY EVERY PAGE AND EVERY
11 ASPECT OF THE EPIDEMIOLOGIC STUDIES.

12 AND HAVING LISTENED TO THE PRESENTATIONS THIS

13 MORNING, I BASICALLY CHECKED EACH ONE OF THEM OFF ONE BY
14 ONE. BECAUSE I THINK DR. GARSHICK, ALLAN, KATHIE, AND
15 TOM, ACTUALLY PRESENTED ALMOST -- ALMOST WITHOUT EXCEPTION
16 EVERY POINT THAT I WOULD HAVE MADE OR SPECULATED ABOUT IN
17 THE CASE OF THE ISSUES OF EXPOSURE. SO I HAVE VERY, VERY
18 LITTLE TO STAY.

19 I CAN MAKE ONE OR TWO COMMENTS, WHICH I DON'T
20 REALLY THINK ARE TERRIBLY HELPFUL, BUT I'LL MAKE THEM
21 ANYWAY BECAUSE I'VE GOT TO SAY SOMETHING.

22 WE'RE TALKING WHEN WE MEASURE EXPOSURE AND WE
23 MAKE CONCLUSIONS FROM EXPOSURE OUTCOME RELATIONSHIPS ABOUT
24 BEHAVIORAL ISSUES, AND WE HAVE TO KEEP IN MIND THAT WHEN
25 WE'RE TALKING ABOUT LUNG CANCER, AND STAN WOULD BE THE
0127

01 FIRST TO POINT OUT IF WE GAVE HIM ANYMORE THAN A SPLIT
02 SECOND OF OPPORTUNITY, THAT WE'RE TALKING ABOUT SMOKING,
03 AND SMOKING IS A VERY DIFFICULT THING TO COMPLETELY ADJUST
04 FOR.

05 SO I WOULD HAVE A CERTAIN LEVEL OF HESITATION
06 THAT WE HAVE ACCURATELY ADJUSTED FOR SMOKING IN ANY OF
07 THESE EVALUATIONS.

08 HOWEVER, IN GENERAL, I THINK THAT THE PROBLEM
09 IS NOT REALLY CONFOUNDING BY SMOKING SO MUCH AS IT IS
10 MISCLASSIFICATION TO SOME EXTENT.

11 SO MY INCLINATION, IF LOOKING AT THE CATEGORIES OF
12 STUDIES THAT HAVE BEEN DONE, IS TO SAY THAT AMONG THE CASE
13 CONTROL STUDIES THERE ARE A COUPLE IN WHICH MAYBE THERE
14 HAVE BEEN OVERESTIMATIONS ON THE BASIS OF SMOKING
15 CONFOUNDING; FOR EXAMPLE, THE ONE IN WHICH THE STUDIES
16 FROM DETROIT IN WHICH COLON CANCER CASES WERE USED AS A
17 CONTROL, COLON CANCER BEING A DISEASE OF WHITE COLLAR
18 WORKERS AND NOT BLUE COLLAR WORKERS.

19 THERE ARE THOSE IN WHICH CONTROLS WERE
20 SELECTED FROM EITHER HOSPITAL PATIENTS OR FROM OTHER
21 DEATHS, IN WHICH THE LIKELIHOOD OF SMOKING RELATED DISEASE
22 IS LIKELY TO HAVE BEEN THERE MORE THAN IT WOULD HAVE BEEN
23 HAD IT BEEN THE GENERAL POPULATION CONTROLS, AND IN THOSE
24 CASES PERHAPS THE RISKS WERE UNDERESTIMATED.

25 AND THEN THERE ARE THE COHORT STUDIES IN
0128

01 WHICH -- I THINK THERE ARE PROBABLY MORE MISCLASSIFICATION
02 THAN ACTUAL CONFOUNDING.

03 BUT WE REALLY DON'T KNOW, AND WE HAVE TO --
04 AS BOTH KATHIE AND TOM POINTED OUT, WE'RE DEALING WITH
05 SURROGATE MEASURES OF EXPOSURE, EVEN THOUGH THEY MAY BE
06 FINELY DIVIDED BY DETAIL AND OCCUPATION.

07 AND THAT MEANS THERE'S GOING BE TO A LOT OF
08 VARIABILITY IN THE ACTUAL DIESEL EXPOSURE WITHIN EACH OF
09 THESE CATEGORIES, AND BY THE SAME TOKEN SOME MEASURE OF
10 VARIABILITY IN THE DEGREE OF SMOKING.

11 THAT WE CAN'T MEASURE. IN OTHER WORDS, YOU
12 CAN MEASURE THE NUMBER OF CIGARETTES, THE CUMULATIVE
13 NUMBER OF CIGARETTES, BUT YOU CAN'T MEASURE THE LENGTH OF
14 THE CIGARETTE THAT'S SMOKED, YOU CAN'T MEASURE THE AMOUNT
15 OF TIME THAT THE CIGARETTE IS KEPT IN THE MOUTH RATHER
16 THAN KEPT IN THE HAND, ET CETERA, ET CETERA, ET CETERA.

17 SO ANYWAY I -- I DON'T THINK IT'S -- IT

18 DOES -- I THINK THE NET EFFECT IS THAT, IF ANYTHING, IT'S
19 REDUCED THE MAGNITUDE OF THE MEASURED EFFECTS.
20 OTHER COMMENT I MIGHT MAKE IS ABOUT -- AS
21 WITH EVERYBODY ELSE, ABOUT THE DOSE-RESPONSE RELATIONSHIP
22 STUDIES THAT WE'RE GOING TO HEAR ABOUT LATER.
23 IF ANYTHING, THESE MISCLASSIFICATION ISSUES
24 WITH SMOKING MAKE THOSE ESTIMATES EVEN MORE DIFFICULT TO
25 ASSESS BECAUSE THERE'S GOING TO BE RELATIONSHIP BETWEEN
0129 DOSE AND THE KINDS OF BEHAVIORAL ISSUES THAT I WAS
02 SPEAKING ABOUT A MOMENT AGO.
03 AND MYSELF, I'M NOT ENTIRELY SURE EVEN WHY WE
04 SPENT A LOT OF TIME DISCUSSING THOSE DOSE-RESPONSE
05 RELATIONSHIPS, AND THE REASON WHY I DON'T KNOW WHY WE DO
06 IS BECAUSE HISTORICALLY, WE DID THAT IN THE -- IN THE
07 ASSESSMENT OF TOXIC AIR CONTAMINANTS VERY EARLY ON BECAUSE
08 WE WERE TRYING TO EXTRAPOLATE FROM ANIMALS, AND IT
09 REQUIRED THESE DOSE-RESPONSE RELATIONSHIPS TO BE LOOKED AT
10 VERY CAREFULLY.
11 WHEN WE'RE STARTING WITH EPIDEMIOLOGIC DATA,
12 IT'S NOT CLEAR TO ME THAT IT'S THAT IMPORTANT,
13 PARTICULARLY SINCE THE GOAL THAT YOU HAVE IN FRONT OF YOU
14 IS TO DECIDE WHETHER OR NOT DIESEL EXHAUST IS A TOXIC AIR
15 CONTAMINANT.
16 AND I THINK WE HAVE ABUNDANT EVIDENCE TO
17 SUGGEST THAT THERE ARE TOXIC ELEMENTS IN DIESEL EXHAUST.
18 WE HAVE ABUNDANT REASON TO BELIEVE THAT IT IS
19 AN AIR CONTAMINANT; AND GIVEN THAT WE'VE LOOKED AT THE
20 RELATIVE RISKS, AND I WOULD CONCUR WITH ALLAN'S VERY BRIEF
21 SUMMARY ESTIMATE OF THE MAGNITUDE OF THE EFFECTS, I THINK
22 YOU'RE GONG TO BE LEFT WITH NO OTHER CONCLUSION BUT TO SAY
23 THAT IT IS A TOXIC AIR CONTAMINANT.
24 THE DIFFICULTY, OF COURSE, THEN COMES AT
25 ANOTHER STAGE IN THE CYCLE, AND I WOULD LIKE TO MAKE VERY
0130 CLEAR THAT IT IS ANOTHER STAGE IN THE CYCLE, AND THAT'S
02 THE REGULATORY PROCESS, THE RISK ASSESSMENT AND
03 QUANTITATIVE RISK ASSESSMENT.
04 SO WITH THAT, I'M GOING TO STOP, JOHN.
05 DR. FROINES: THANK YOU VERY MUCH. THANK YOU VERY
06 MUCH.
07 HE ALWAYS HAS SOMETHING GOOD TO SAY. NO
08 MATTER WHAT.
09 RATHER THAN SORT OF ASKING KATHIE TO TALK
10 ABOUT ALLAN TO TALK ABOUT ERIC TO TALK ABOUT TOM SMITH, I
11 DON'T EVEN KNOW IF TOM SMITH IS HEARING US. IS HE? CAN
12 HE SPEAK TO US?
13 DR. TOM SMITH: I AM. I'M HIDING BACK HERE. CAN
14 YOU HEAR ME? I DEFINITELY AM LISTENING, AND IT WAS
15 TREMENDOUSLY INTERESTING.
16 DR. FROINES: GREAT.
17 DR. GLANTZ: HE CAN WALK INTO THE CAMERA SINCE WE
18 NOW HAVE A GREAT PICTURE OF THIS ROOM.
19 DR. FROINES: HOW L.A.
20 DR. TOM SMITH: RIGHT. AND YOU THOUGHT I HAD LEFT,
21 OH, MAN.
22 DR. FROINES: THE QUESTION THAT WE HAVE TO CONCLUDE

23 OUT OF THIS MEETING IS NOT SO MUCH ABOUT DIESEL, BUT
24 WHETHER THIS IS THE FUTURE. IT SEEMS IT MAY BE, BUT THERE
25 MAY BE SOME TINKERING WE HAVE TO DO WITH IT.

0131

01 DR. TOM SMITH: I THINK SO. YOU'VE GOT TO GET
02 ACTORS.
03 DR. FROINES: ACTORS. WHO WOULD YOU LIKE TO PLAY
04 YOU?
05 DR. TOM SMITH: HOW ABOUT ROBERT DUVALL?
06 DR. GLANTZ: I WAS THINKING MATT DAMON.
07 DR. FROINES: WHY DON'T WE OPEN IT UP FOR
08 DISCUSSION BETWEEN THE TWO SIDES OF THE TABLE AND
09 INCLUDING OUR HOLLYWOOD PARTICIPANT BACK THERE.
10 PAUL?
11 DR. BLANC: ALLAN, I WOULD TO ASK YOU EXPAND A
12 LITTLE BIT ON A COMMENT THAT YOU SAID AS AN ASIDE ALMOST
13 BECAUSE OF THE TIME CONSTRAINTS THAT YOU HAD REGARDING THE
14 LIKELIHOOD THAT COMPLICATED MULTI-VARIATE PREDICTIVE
15 MODELS OF THE DOSE-RESPONSE THAT INCLUDE AGE IN THE MODEL
16 ARE LIKELY TO FALL -- GIVE A FALSE NEGATIVE-DOSE-RESPONSE
17 BECAUSE OF THE COLLINEARITY BETWEEN THE AGE AND THE YEARS
18 ELAPSED SINCE FIRST EXPOSURE.
19 MY QUESTION IS -- AND I UNDERSTAND THAT THAT
20 WOULD OBVIOUSLY BE A PROBLEM FROM A THEORETICAL POINT OF
21 VIEW.
22 IT -- IN YOUR READING OF THE DRAFT DOCUMENT
23 AS IT CURRENTLY EXISTS, DO YOU BELIEVE THAT SUCH
24 COLLINEARITY HAS INTERFERED WITH ANY OR ALL OR SOME OF THE
25 DOSE-RESPONSE MODELS THAT ARE PRESENTED VIS-A-VIS THE

0132

01 HUMAN EPIDEMIOLOGIC DATA?
02 DR. ALLAN SMITH: I HOPE -- I HAD HOPED NOBODY
03 WOULD ASK ME A QUESTION, BUT TO EXPLAIN WHAT I WAS GETTING
04 AT, FIRSTLY, I -- ONCE WHEN I STARTED IN FULL TIME IN
05 EPIDEMIOLOGY RESEARCH ABOUT 25 YEARS AGO, I THOUGHT THAT
06 MULTI-VARIATE MODELS WERE GOD'S GIFT TO MEDICINE AND WOULD
07 SOLVE EVERYTHING.
08 I DID QUITE A BIT WITH THEM IN MY
09 DISSERTATION WORK AND BECAME RAPIDLY DISILLUSIONED WITH
10 THE WAY NUMBERS WOULD JUMP AROUND.
11 I WAS THEN WORKING ON BLOOD PRESSURE IN WHICH
12 I HAD SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE,
13 CHOLESTEROL, BODY WEIGHT, AGE, AND I JUST NOTED THAT
14 EVERYTHING WAS HIGHLY UNSTABLE, PARTICULARLY IF YOU DID
15 SOMETHING A LITTLE BIT WRONG OR TWEAKED THE MODEL.
16 SO I BECAME VERY SUSPICIOUS OF MODELS, AND
17 WHAT I TEACH MY STUDENTS IS THAT FIRST WORK OUT WHAT THE
18 RESULTS ARE ON SIMPLE STRATIFIED ANALYSIS, AND THEN ONCE
19 YOU KNOW WHAT THE RESULTS ARE GOING TO BE MORE OR LESS,
20 THEN DO MULTI-VARIATE MODELS, BUT MAKE SURE YOU KNOW THE
21 ANSWER FIRST BECAUSE OTHERWISE THEY ARE DANGEROUS.
22 NOW, WITH REGARD THOUGH, COMING BACK TO THE
23 DOCUMENT, MY COMMENT WAS IN PART BECAUSE I -- I THINK
24 THAT -- AND I'M GLAD DUNCAN THOMAS IS HERE BECAUSE HE'S
25 MORE AN EXPERT TO COMMENT ON THIS.

0133

01 BUT THE -- YOU -- EACH OF THESE MODELS MAKE

02 CERTAIN ASSUMPTIONS. I ACTUALLY THOUGHT THAT THE MODEL
03 THAT DR. GARSHICK USED ON HIS COHORTS, THAT HE WAS FINE
04 AND APPROPRIATE. IT'S -- IT'S WHEN THOUGH YOU START
05 PLAYING AROUND WITH DIFFERENT WAYS OF JUGGLING AGE,
06 JUGGLING DURATION OF EXPOSURE IN A COHORT THAT HAS A FIXED
07 DATE START OF EXPOSURE, WHICH THE PROBLEM IN THAT COHORT
08 TO ME IT IS NOT EXACTLY FIXED AS KATHIE WAS POINTING OUT.
09 THE EXPOSURE MORE OR LESS STARTED FOR
10 EVERYBODY ABOUT THE SAME TIME, WHICH IS NOT TYPICAL OF
11 COHORT STUDIES.
12 SO THEN YOU HAVE YOUR EXPOSURE VARIABLE MUCH
13 MORE DEPENDENT THAN THIS STUDY ON CALENDAR TIME, AND ONCE
14 YOU THEN GET THAT MIX IN, I THINK THERE'S A WAY THAT
15 DR. KENNY CRUMP DID A VARIETY OF MODELS THAT ALL SHOWED
16 DIFFERENT SLOPES. I WOULD SAY TO ME THAT IS NOT EVIDENCE
17 AT ALL OF ANYTHING. THAT'S WHAT I MIGHT EXPECT IF YOU
18 PLAY AROUND WITH THESE MODELS.
19 WITH REGARD THOUGH TO THE -- MY COMMENT ON
20 THE DOCUMENT, I THINK THAT, IN MY VIEW, THERE IS EVIDENCE
21 OF DURATION AND EXPOSURE TRENDS WITHIN THAT PARTICULAR
22 STUDY, AND I PERSONALLY WOULDN'T GO TOO MUCH FURTHER THAN
23 THAT.
24 BUT NEVERTHELESS I WOULD -- DO BELIEVE THAT
25 THE WORK THAT STAN DAWSON HAS DONE ALSO WOULD SUPPORT AND
0134 DOES SUPPORT THAT THERE ARE SOME TRENDS.
02 NOW, I'VE GIVEN A LONG ANSWER, AND I THINK IT
03 IS A COMPLICATED QUESTION. WE COULD DEBATE A LONG TIME,
04 BUT I WAS REALLY GETTING AT, I GET WORRIED IF PEOPLE PUT
05 TOO MUCH CONFIDENCE IN MODERN ANALYSIS; AND SECONDLY, THEY
06 GET TOO WORRIED IF JUGGLING THE MODELS IN DIFFERENT WAYS
07 PRODUCES QUITE DIFFERENT RESULTS.
08 DR. FROINES: PETER IS NEXT.
09 DR. WITSCHI: YEAH, I HAVE A QUESTION TO KATHIE
10 PROBABLY.
11 I LIVE IN DAVIS ON THE WRONG SIDE OF THE
12 TRACKS, AND SO I SEE QUITE A FEW OF THOSE OLD DIESEL
13 ENGINES GOING BY.
14 THE QUESTION I HAVE, WHAT DO WE KNOW ABOUT
15 THE FLEET, THE CAR FLEET, TRUCKS AND PASSENGER CARS? DO
16 WE HAVE THE SAME PHENOMENON, MOSTLY OLD MODELS, OR HOW HAS
17 THIS CHANGED OVER THE TIMES?
18 DR. HAMMOND: IS YOUR -- IS YOUR QUESTION
19 AUTOMOBILES, CARS?
20 DR. WITSCHI: YES, YES. I MEAN, HOW MANY OF THE
21 CARS OF THE DIESEL FLEET THAT'S STAYED AROUND, WHICH WOULD
22 BE THE EARLIER TECHNOLOGY THAT WAS MUCH MORE DIRTY THAN
23 WHAT'S PRESENT TODAY?
24 DR. HAMMOND: SHALL WE SAY AUTOMOBILES ARE
25 INTERMEDIATE BETWEEN P.C.'S AND LOCOMOTIVES? AUTOMOBILES
0135 ARE INTERMEDIATE IN LIFE SPAN.
02 DR. FROINES: IS PETER -- IS PETER TRYING TO DECIDE
03 WHETHER TO MOVE ACROSS THE TRACKS OR NOT?
04 DR. HAMMOND: I THINK -- FIRST OF ALL, I REALLY --
05 I HAVE NEVER STUDIES THE LENGTH OF CARS. SO I REALLY
06 PROBABLY CAN'T ANSWER THAT. SO IT'S, YOU KNOW --

07 DR. WITSCHI: I'M TALKING ABOUT CARS, ABOUT TRUCKS,
08 ALL THE MOBILE SOURCES OTHER THAN LOCOMOTIVES. DO YOU
09 HAVE ANY INFORMATION?
10 DR. HAMMOND: NOW, THE REASON I WAS TALKING ABOUT
11 THE LOCOMOTIVES, THE PURPOSE OF THAT WAS TO TRY TO
12 INTERPRET THE EXPOSURES IN THE STUDY AND HOW THOSE
13 EXPOSURES CHANGED OVER TIME.
14 I THINK IN TERMS OF THE CAR FLEETS, THE TRUCK
15 FLEETS AND ALL OF THAT, THAT'S WHERE I WOULD TURN TO --
16 SAY, TO BARBARA, FOR INSTANCE, WHO HAS DONE SOME WORK ON
17 THAT, OR PEOPLE WHO HAVE LOOKED AT -- AND THERE HAVE BEEN
18 STUDIES THAT I'VE SEEN, YOU KNOW, THAT CLAIM THAT MOST OF
19 THE PARTICLE EXPOSURES ARE COMING FROM OLDER VEHICLES.
20 BUT THAT -- THAT'S OTHER SOURCE OF DATA THAT
21 I CAN'T TELL YOU ABOUT.
22 DR. FROINES: JIM.
23 DR. SEIBER: I HAD A QUESTION FOR ALLAN.
24 GOING BACK TO YOUR SORT OF BRIEF CALCULATION
25 AT THE END OF YOUR PRESENTATION WHEN YOU TOOK
0136
01 50 MICROGRAMS PER CUBIC METER AND EXTRAPOLATED DOWN, WAS
02 THAT -- IS THAT KIND OF A LINEAR EXTRAPOLATION THAT YOU
03 DID?
04 DR. ALLAN SMITH: YES, IT WAS. AND OF COURSE, AT
05 THE TIME I TOOK THAT 50 NUMBER, I HADN'T HEARD
06 KATHIE HAMMOND'S PRESENTATION, BUT IT'S SORT OF IN THE
07 MIDDLE THERE SOMEWHERE OF THOSE ESTIMATES, BUT YEAH. THE
08 FUNDAMENTAL ASSUMPTION IN COMING WITH THE RISK ESTIMATE I
09 DID IS THAT THERE ISN'T A THRESHOLD AND THINGS ARE MORE OR
10 LESS LINEAR.
11 THE ONLY -- THE BASIS I GET FOR DOING THAT IS
12 IN THE ESTABLISHED HUMAN CARCINOGENS, WE HAVE NOT
13 GENERALLY ESTABLISHED THAT THERE ARE THRESHOLDS. IN FACT,
14 OVER THE YEARS, WE KEEP FINDING IF THEY ARE PROPOSED, THE
15 PROPONENTS PROPOSE THEM LOWER AND LOWER AS MORE DATA COMES
16 IN.
17 SO YOU ARE CORRECT. IT'S ASSUMING A LINEAR
18 EXTRAPOLATION. THERE'S NO BASIS FOR IT IN THE
19 EPIDEMIOLOGICAL DATA. IT'S BASED IN THE DIESEL AREA THAT
20 IT IS LINEAR DOWN AT THOSE LEVELS.
21 SO NEVERTHELESS, IF ONE LOOKS HISTORICALLY AT
22 ESTABLISHED HUMAN CARCINOGENS, THEY ARE ROUGHLY LINEAR.
23 THE FINDING FROM SOMEBODY PASSIVE SMOKING MAY BE A BIT
24 SUPRALINEAR, AND THERE ARE ONES OF ARSENIC INHALATION
25 WHICH IS SUPRALINEAR, AND THEN THERE ARE SOME THAT ARE
0137
01 SOMEWHAT SUBLINEAR, BUT THEY ARE PRETTY CLOSE TO LINEAR,
02 MOST OF THEM.
03 DR. SEIBER: SO IF YOU USE THE -- I THINK THE
04 O.E.H.H.A. -- THE DRAFT REPORT A.R.B. O.E.H.H.A. USED AS A
05 STATE-WIDE AVERAGE EXPOSURE OF -- LET'S SEE 2.1 IN 1990,
06 1.5 IN 1995 AND 1.3 IN THE YEAR 2000 AS AN ESTIMATE, WE
07 WOULD SIMPLY ADJUST YOUR CALCULATION -- IT'S STILL A
08 SIGNIFICANT NUMBER OF EXCESS CANCERS PER MILLION --
09 DR. ALLAN SMITH: RIGHT.
10 DR. SEIBER: -- BUT NOT -- NOT AS GREAT AS THE
11 NUMBER THAT YOU USED, WHICH I THINK WOULD HAVE BEEN

12 2,000 --
13 DR. ALLAN SMITH: WELL, I USED A LEVEL OF FOUR
14 MICROGRAMS --
15 DR. SEIBER: -- PER MILLION.
16 DR. ALLAN SMITH: -- WOULD BE THE CUBE FOR URBAN
17 AREAS. SO I WOULDN'T SAY THAT CHANGE MADE VERY MUCH
18 DIFFERENCE. THESE ARE ORDER OF MAGNITUDE ESTIMATES. I'M
19 SURE YOU'RE RIGHT.
20 DR. SEIBER: OKAY. THANK YOU.
21 DR. FROINES: DOES -- IS KATHIE'S DATA INCLUDED IN
22 THE REPORT? HER AND -- AND TAKING THESE TWO COMMENTS, IS
23 -- ARE THOSE ESTIMATES OF RISK ASSOCIATED WITH THOSE
24 EXPOSURE ESTIMATES IN THE REPORT? AND DO THEY NEED TO BE?
25 DR. ALEXEEFF: THE -- THE GIST OF KATHIE'S
0138
01 COMMENTS ARE IN THE REPORT BASED UPON THE RANGE OF
02 EXPOSURE, SORT OF PATTERNS THAT ARE THERE.
03 SO WE DON'T HAVE, FOR EXAMPLE, THE SUGGESTION
04 OF -- OF SUBTRACTING THE OUTDOOR AIR RISK NUMBER AS BEING
05 THE BEST ESTIMATE.
06 INSTEAD, WE HAVE THE FIRST TWO PROPOSALS SHE
07 HAD ON THERE. DO NOTHING OR DO EVERYTHING. SO WE'VE
08 BRACKETED WHAT THE EXPOSURE WOULD BE.
09 DR. FROINES: DALE, ARE YOU GOING TO TALK TO THAT
10 AT SOME POINT?
11 DR. HATTIS: YEAH. I'VE GOT BASICALLY -- I THINK I
12 AGREE WITH KATHIE THAT IN FACT THAT OUTDOOR BACKGROUND IS
13 LIKELY THE BEST ANSWER. IT CHANGES THE NUMBER VERY
14 MODESTLY IN THE DIRECTION OF LOWERING THE EXPECTED
15 POTENCY.
16 I WOULD LIKE TO SEE IN ADDITION TO
17 KATHIE'S -- I THINK WHAT'S IN THE DOCUMENT AT THE MOMENT,
18 TO ANSWER YOUR QUESTION, IS A BRACKET -- AN OVERALL
19 BRACKETING OF THE POSSIBLE INTERPRETATIONS OF THE CASE
20 CONTROL STUDY DATA IN -- AND THE META-ANALYSIS.
21 I WOULD -- I WOULD -- I THINK IT WOULD BE
22 INTERESTING AS A SUPPLEMENT TO INCLUDE THE MORE SPECIFIC
23 ESTIMATES THAT YOU'VE MADE OF THE DIFFERENT CATEGORIES OF
24 WORKERS AND THE IMPLICATIONS OF THOSE FOR THE
25 META-ANALYSIS CALCULATED POTENCY NUMBERS.
0139
01 DR. FROINES: SO EVERYBODY WHO'S HERE IN THE
02 AUDIENCE, STICK AROUND BECAUSE DALE HATTIS HAS SOMETHING
03 NEW TO SAY, BUT IT'S GOING TO BE A FEW HOURS FROM NOW.
04 STAN?
05 DR. GLANTZ: I'D LIKE TO -- YOU KNOW, YOU PUT
06 GRAPHS IN FRONT OF ME AND I GO NUTS, BUT THE -- COULD YOU
07 PUT UP DR. GARSHICK'S -- THE LAST GRAPH, THE BLUE ONE. I
08 WANT TO ASK A COUPLE QUESTIONS. NO, NO. IT WAS THE BLUE
09 ONE WITH THE WEIRD EXTRAPOLATION ON IT. YEAH.
10 DR. BLANC: THE MONTE CARLO PROJECTION, WAS THAT
11 RIGHT?
12 DR. GLANTZ: WELL, WELL -- YEAH, THAT ONE.
13 I -- I MEAN, NOT TO BE RUDE OR ANYTHING, BUT
14 THAT LOOKS LIKE A PRETTY STRANGE LINE TO DRAW THROUGH THAT
15 GRAPH. I MEAN, THE WAY I WOULD INTERPRET THAT TOTALLY
16 NAIVELY IS THAT WHAT IT'S SHOWING IS THAT A LITTLE BIT OF

17 EXPOSURE IS BAD AND THEN -- AND THEN, YOU KNOW, YOU GET
18 SORT OF A SATURATION EFFECT OR SOMETHING.
19 I MEAN, CONVINCE ME THAT RATHER THAN DRAWING
20 A LINE WHICH DOESN'T LOOK ANYTHING LIKE THE DATA POINT.
21 DR. GARSHICK: THIS LINE HERE. THIS IS BASED ON IF
22 YOU MODEL CUMULATIVE YEARS OF EXPOSURE, AND THIS IS IF YOU
23 DO THE CATEGORICAL ANALYSIS, SHOWING IF YOU ANCHOR -- IF
24 YOU ANCHOR THE YEARS OF EXPOSURE BASED UPON CUMULATIVE
25 YEARS --

0140
01 DR. GLANTZ: WAIT. NO.
02 DR. GARSHICK: -- YOU GET THIS POINT AND THAT
03 POINT.
04 DR. GLANTZ: I UNDERSTAND THAT.
05 DR. GARSHICK: BUT THAT'S NOT -- I DIDN'T ATTEMPT
06 TO PUT A LINE THROUGH THIS.
07 DR. GLANTZ: NO. THAT'S FINE. BUT I WANT TO MAKE
08 SURE I UNDERSTAND THIS. WHAT YOU DID IS YOU HAD -- IF YOU
09 LOOK AT THE ORANGE POINTS AND THE -- AND THE ERROR BARS,
10 THOSE WERE THE RISKS THAT YOU ESTIMATED FOR A GROUP OF
11 PEOPLE WHO HAD LIKE ZERO TO FIVE YEARS --
12 DR. GARSHICK: ZERO TO SEVEN, RIGHT, EXACTLY.
13 DR. GLANTZ: AND THEN THE NEXT ONE WAS SEVEN TO TEN
14 AND STUFF LIKE THAT --
15 DR. GARSHICK: EXACTLY.
16 DR. GLANTZ: OKAY. WELL, IF THAT'S THE CASE, IF
17 YOU JUST USE THE EYEBALL METHOD, WHICH I WAS CRITICIZING
18 JOE MAUDERLY FOR DOING EARLIER, THE -- IT LOOKS TO ME LIKE
19 WHAT YOU'RE SHOWING THERE IS THAT EVEN THE SHORT-TERM
20 EXPOSURES YOU GET AN INCREASE IN RISK, AND THEN IT SORT OF
21 STABILIZES.

22 AND SO A LITTLE BIT OF EXPOSURE IS ALL YOU
23 REALLY NEED TO HAVE AN EFFECT, AND THEN LONGER-TERM
24 EXPOSURES AREN'T REALLY DOING ALL THAT MUCH.
25 I MEAN, THAT WOULD BE MY INTERPRETATION JUST

0141
01 SEEING THIS GRAPH FOR THE FIRST TIME TODAY.
02 DR. GARSHICK: THE QUESTION IS WHAT'S CAUSING
03 THIS. DOES THIS REPRESENT THE EFFECT OF JUST A FEW YEARS
04 OF EXPOSURE? THAT WOULD INDEED MAKE DIESEL A RELATIVELY
05 POTENT CARCINOGEN.
06 DR. GLANTZ: YEAH.
07 DR. GARSHICK: DOES IT REPRESENT THE EFFECT OF --
08 OF COMPETING EXPOSURES FROM OTHER COMBUSTION PRODUCTS
09 DURING THE STEAM ERA? DOES IT REFLECT --
10 DR. GLANTZ: WELL, NO --
11 DR. GARSHICK: -- THE HOMOGENEITY OF SMOKING
12 HABITS --
13 DR. GLANTZ: RIGHT.
14 DR. GARSHICK: -- OR DOES IT REFLECT THE LACK OF
15 INCLUDING LATENCY THAT THESE DEATHS ACTUALLY OCCURRED
16 THROUGHOUT THE YEARS OF THE COHORT, AND MAYBE WITH
17 INCREASING LATENCY, YOU KNOW, GIVEN A FIXED EXPOSURE IS AN
18 INCREASE IN RISK.
19 SO THERE IS A NUMBER OF EXPLANATIONS.
20 DR. GLANTZ: WELL, I UNDERSTAND THAT, BUT BY
21 PRESUMABLY BY PUTTING THE GRAPH UP IN FRONT OF US, YOU

22 DON'T THINK YOU'RE PUTTING SOMETHING SILLY UP THERE?
23 DR. GARSHICK: NO.
24 DR. GLANTZ: OKAY. I WOULD PRESUME --
25 DR. GARSHICK: I -- I'M -- I'M LOOKING FOR --

0142
01 I'M NOT SURE. THIS IS ELEVATED AT THAT POINT. I GUESS
02 MY POINT IS THIS IS VERY DISSIMILAR TO WHAT'S IN THE
03 DOCUMENT REGARDING THE ANALYSIS OF YEARS OF EXPOSURE.
04 DR. GLANTZ: RIGHT. WELL, I'M NOT TALKING ABOUT
05 THE DOCUMENT. I'M TRYING TO UNDERSTAND THIS GRAPH. I
06 MEAN, EVEN IF YOU THROW AWAY THE FIRST POINT, OKAY, IT'S
07 DRAWING THAT YELLOW LINE STILL DOESN'T SEEM TO MAKE A LOT
08 OF SENSE TO ME. I MEAN, WHAT THIS IS SHOWING --
09 DR. GARSHICK: RIGHT. WE DON'T THINK THIS IS THE
10 RIGHT DOSE-RESPONSE. WE ARE SHOWING HOW IT CAN HAPPEN IF
11 YOU MODEL CUMULATIVE EXPOSURE. THAT'S ALL WE'RE SHOWING,
12 THE DIFFERENCE BETWEEN LINES --
13 DR. GLANTZ: OKAY. BUT WOULD A RAT -- ASSUMING
14 THAT -- THAT YOUR ANALYSIS AND -- YOU KNOW, IT WAS
15 COMPETENTLY DONE, AND WHICH I'M HAPPY TO ASSUME, AND THAT
16 YOU CONTROLLED APPROPRIATELY FOR ALL THOSE OTHER THINGS
17 THAT YOU MENTIONED --
18 DR. GARSHICK: RIGHT.
19 DR. GLANTZ: -- I MEAN, WOULDN'T A REASONABLE
20 INTERPRETATION OF THIS SLIDE HERE BE THAT YOU GET A HIGH
21 SHORT-TERM POTENCY, AND THEN MAYBE YOU DON'T GET -- MAYBE
22 THERE IS SOME SYSTEM THAT JUST GETS SATURATED.
23 DR. GARSHICK: IF YOU'RE -- I MEAN, WE'RE LOOKING
24 FOR REASONS FOR THIS POINT AND THAT MAY BE --
25 DR. GLANTZ: NO, I MEAN, I'M LOOKING FOR REASONS --

0143
01 NO. I'M LOOKING FOR REASONS FOR ALL THE POINTS.
02 DR. GARSHICK: WELL, THE RISK IS OVERALL ELEVATED,
03 BUT THE CREWDNESS OF THE EXPOSURE DATA IS HARD TO SORT OUT
04 THE EXACT DOSE-RESPONSE JUST USING YEARS --
05 DR. GLANTZ: NO, BUT -- NO, NO, NO. YOU'RE MISSING
06 THE POINT I'M MAKING, AND THAT IS, IF YOU LOOK -- IF YOU
07 LOOK AT THE ALL THE POINTS, THE FACT THAT THE FIRST POINT
08 IS A LITTLE HIGHER THAN THE REST ISN'T THE POINT THAT I'M
09 CONCERNED ABOUT HERE.
10 THE POINT THAT I'M CONCERNED ABOUT HERE IS IT
11 LOOKS LIKE YOU GET A FAIRLY RAPID INCREASE IN RISK AT LOW
12 YEARS OF EXPOSURE, AND THEN IT LOOKS KIND OF LIKE IT
13 PLATEAUS. I MEAN, I'M NOT TALKING ABOUT THE REPORT. I'M
14 TALK ABOUT THIS SLIDE.
15 DR. GARSHICK: RIGHT. OKAY. OKAY.
16 DR. GLANTZ: SO I MEAN, I THINK -- IS -- WOULD THAT
17 NOT BE A REASONABLE INTERPRE- -- LET'S JUST --
18 DR. GARSHICK: THAT WOULD BE ONE INTERPRETATION,
19 RIGHT.
20 DR. GLANTZ: AND WHAT'S WRONG -- I MEAN, WHAT'S
21 WRONG WITH THAT INTERPRETATION?
22 DR. GARSHICK: THE INTERPRETATION IS THAT IF YOU
23 ARE LOOKING FOR A SINGLE SLOPE BASED ON THE DATA IN THE
24 STUDY, THERE ARE A LOT OF UNCERTAINTIES.
25 NOW, THE TERMS OF THE STUDY BEING POSITIVE

0144

01 AND NEGATIVE. I NEVER SAID THE STUDY WAS NEGATIVE. I'M
02 SAYING -- I'M COMMENTING ON THE ABILITY TO DEFINE A
03 DOSE-RESPONSE, AND IT'S -- IT'S VERY DIFFICULT.
04 AND I'M -- THIS IS ANOTHER WAY OF LOOKING AT
05 IT. THE DOCUMENT LOOKED AT IT ANOTHER WAY. AND I -- I
06 THINK THAT THIS GETS TO -- I MEAN, TO DECIDE IF THE
07 TOXIC -- THE AIR CONTAMINANT DOESN'T DEPEND ON WHETHER YOU
08 CAN FIT A SLOPE THROUGH THESE DATA.
09 DR. GLANTZ: RIGHT. BUT WHAT I'M SAYING IS, BASED
10 ON THIS DATA, WOULDN'T IT BE -- WOULD YOU SAY THAT A
11 BETTER THING TO DO THAN TO FIT A SINGLE SLOPE, WHICH, YOU
12 KNOW, LOOKING AT THIS GRAPH IS SILLY --
13 DR. GARSHICK: RIGHT.
14 DR. GLANTZ: -- TO -- TO SAY, OKAY. WELL, WHAT WE
15 SHOULD DO IS SAY WE'VE GOT SOME KIND OF SATURATING PROCESS
16 WHERE YOU GET A HIGH TOXICITY AT LOW EXPOSURES, AND THEN
17 IT TENDS TO FLATTEN OUT.
18 DR. GARSHICK: I MEAN, WE'RE SPECULATING ABOUT THE
19 BIOLOGY HERE. THAT'S THE ONE THING THAT IS MISSING FROM
20 ALL THESE DISCUSSIONS, AND I MEAN, IF WE'RE SAYING --
21 DR. GLANTZ: YEAH, BUT THAT'S NOT THE QUESTION I'M
22 ASKING.
23 DR. GARSHICK: NO, NO. BUT HOW YOU INTERPRET THESE
24 POINTS DEPENDS ON BIOLOGY OF WHAT YOU'RE STUDYING.
25 DR. GLANTZ: NO. I --
0145 DR. GARSHICK: IT IS PLAUSIBLE THAT A FEW YEARS OF
01 DIESEL CAN CAUSE THIS AMOUNT OF RISK? IS IT PLAUSIBLE? I
02 MEAN, THAT'S A QUESTION.
03 DR. GLANTZ: WELL, BUT I'M -- SEE, IF YOU LOOK
04 AT -- IF YOU LOOK AT NOW, YOU KNOW, SOMEONE DANGLED THE
05 WORD SMOKING IN FRONT OF ME, BUT IF YOU LOOK AT -- IF YOU
06 LOOK AT PASSIVE SMOKING AND HEART DISEASE, YOU SEE
07 SOMETHING VERY MUCH LIKE THIS, WHERE YOU GET A BIG
08 INCREASE AT LOW DOSES, AND THEN IT TENDS IT PLATEAU.
09 SO I MEAN, I REALIZE THAT HEART DISEASE ISN'T
10 CANCER, AND CIGARETTE SMOKE ISN'T DIESEL FUMES, BUT IF YOU
11 LOOK AT THE ERROR BARS THAT YOU'VE DRAWN ON THERE, OKAY,
12 THEY TEND TO -- THERE IS A LOT OF OVERLAP.
13 DR. GARSHICK: THERE IS OVERLAP.
14 DR. GLANTZ: AND SO IT SEEMS TO ME RATHER THAN
15 FOCUSING ON THE FACT THAT THAT FIRST POINT IS ELEVATED,
16 WHICH MAY JUST SIMPLY BE STATISTICAL UNCERTAINTY, I MEAN,
17 WOULDN'T A REASONABLE CONCLUSION BASED ON THE EVIDENCE
18 THAT YOU PRESENTED HERE THAT YOU HAVE A HIGH TOXICITY WITH
19 LOW EXPOSURES, AND THEN IT MIGHT BE A DECAYING -- OR A
20 SATURATING EXPONENTIAL DOSE-RESPONSE.
21 DR. GARSHICK: THE EXPOSURES HERE MAY HAVE BEEN
22 DIFFERENT THAN THE EXPOSURES ACCUMULATED BY THIS GROUP IN
23 TERMS OF INTENSITY AND THIS SUPPOSES WHAT YOU'RE SAYING --
24 I KNOW SOMETHING ABOUT THE BIOLOGY OF HOW IT BEHAVES IN
0146 HUMANS. ALL I'M SAYING IS THAT THE SLOPE IS UNCERTAIN,
01 BUT THE WHOLE RISK APPEARS TO BE ELEVATED.
02 DR. GLANTZ: YEAH. BUT I MEAN, WOULD YOU SAY --
03 WOULD YOU SAY BASED ON THIS -- AND I DON'T WANT TO BEAT A
04 DEAD HORSE, AND IF YOU THINK -- YOU -- YOU'RE THE ONE WHO

06 PUT THE GRAPH UP --
07 DR. GARSHICK: RIGHT, RIGHT.
08 DR. GLANTZ: -- OKAY? WOULD A REASONABLE MODEL TO
09 ASSUME, INSTEAD OF IT BEING A STRAIGHT LINE HAD A
10 SATURATED EXPONENTIAL WHERE THE THING GOES UP QUICKLY, AND
11 THEN TENDS TO GO UP MORE SLOWLY AT THE HIGHER REALMS?
12 DR. GARSHICK: I MEAN, YOU COULD PROBABLY FIT A
13 SINGLE MODEL TO THIS. I'M NOT SURE HOW TO INTERPRET IT IN
14 LIGHT OF THE BIOLOGY WHAT WE KNOW SO FAR WHICH ISN'T VERY
15 MUCH IN HUMANS.
16 DR. GLANTZ: BUT ANYWAY. OKAY. WELL, I HAD ONE
17 OTHER QUESTION FOR YOU JUST BECAUSE --
18 DR. TOM SMITH: COULD I MAKE ONE COMMENT ON THAT?
19 DR. FROINES: WAIT A SECOND.
20 DR. GLANTZ: I'M SORRY.
21 DR. FROINES: IS THAT TOM?
22 DR. TOM SMITH: YEAH.
23 DR. FROINES: GO AHEAD.
24 DR. TOM SMITH: JUST ONE -- ONE COMMENT ON THAT.
25 I THINK IT'S IMPORTANT TO REMEMBER THAT YEARS
0147
01 ARE NOT EXPOSURE. YEARS ARE ONLY PART OF THE EQUATION,
02 AND IF YOU PUT SOME ERROR BARS AROUND HOW WELL YEARS
03 REPRESENT EXPOSURE, NAMELY, THE ERROR BARS I WAS TALKING
04 ABOUT ON THE EXPOSURE SCALE, I THINK YOU MIGHT DISCOVER
05 THAT THOSE POINTS, IN FACT, WERE NOT TERRIBLY DIFFERENT
06 FROM ONE ANOTHER OVERALL.
07 DR. GLANTZ: OKAY. BUT THAT --
08 DR. GARSHICK: NO, I THINK THAT'S RIGHT. I THINK
09 IT'S QUITE -- THEY ARE QUITE SIMILAR, THE POINTS, AND THE
10 ISSUE IS JUST ILLUSTRATING THAT FITTING THE SINGLE SLOPE
11 USING YEARS OF EXPOSURE IS DIFFICULT IN THIS DATA.
12 SO THAT'S THE ONLY POINT TO THIS, AND I'M NOT
13 SURE WHAT THE INTERPRETATION AT THIS POINT REALLY IS. BUT
14 IT GOES TO WHAT YOU SAID AS WELL AS SOME OTHER --
15 DR. BLANC: CAN I JUST CLARIFY SOMETHING FOR A
16 SECOND IN THE CONTEXT OF DISCUSSION?
17 I WASN'T INCORRECT, THOUGH, WHEN YOU
18 PRESENTED YOUR ORIGINAL ANALYSIS, IT SHOWED THAT THE
19 LONGER THAT HAD ELAPSED FROM EXPOSURE, THE MORE RISK YOU
20 HAD, AND YOU ALSO SHOWED THAT THE HIGHER EXPOSURE JOBS HAD
21 MORE RISK.
22 SO YOU HAD TWO DIFFERENT WAYS OF COMING AT
23 THE ISSUE OF WAS THERE A DOSE-RESPONSE, WHICH SHOWED THERE
24 WAS A DOSE-RESPONSE; IS THAT CORRECT?
25 DR. GARSHICK: IN THE COHORT STUDY --
0148
01 DR. BLANC: IN THE COHORT STUDY; IS THAT CORRECT?
02 DR. GARSHICK: -- THE WORKERS AGED 44 TO 59 HAD THE
03 HIGHEST RISK OF DYING OF LUNG CANCER.
04 THE PROBLEM CAME IN SORTING OUT
05 DOSE-RESPONSE, AND THE POINT THAT WAS DRIVING THAT
06 REGRESSION, THE 15- TO 17-YEAR-OLD AGE GROUP IS THE GROUP
07 WHERE THE DEATHS ONLY COULD HAVE OCCURRED DURING THE YEARS
08 OF MISSING DEATHS. ALL RIGHT? SO THAT POINT IS VERY
09 UNSTABLE.
10 AND FURTHERMORE, WHEN YOU DO ADJUST FOR

11 ATTAINED AGE AND CALENDAR YEAR THAT THE -- THAT ELEVATED
12 RISK DISAPPEARS, AND KENNY CRUMP'S WORK --
13 DR. BLANC: WE'RE NOT TALKING ABOUT KENNY CRUMP'S
14 WORK RIGHT NOW.
15 DR. GARSHICK: EXACTLY, BUT YOU'RE --
16 DR. BLANC: YOUR SIMPLE MODEL SHOWED THAT THE
17 PEOPLE WHO HAD THE LONGEST TIME ELAPSED FROM FIRST
18 EXPOSURE, ARE THE MOST CHANCE TO GET CANCER, GOT CANCER.
19 DR. GARSHICK: THERE'S TWO MODELS. ALL RIGHT? THE
20 FIRST MODEL IS JOB IN '59 --
21 DR. BLANC: RIGHT.
22 DR. GARSHICK: -- AND THAT SHOWED IN THE JOB GROUP
23 WHO HAD THE MOST FUTURE CHANCE OF WORKING DIESEL ARE MOST
24 LIKELY TO DIE OF LUNG CANCER --
25 DR. BLANC: AND ALSO THE PEOPLE WHO HAD THE HIGHEST
0149
01 EXPOSURE JOB --
02 DR. GARSHICK: LET ME FINISH, LET ME FINISH.
03 THE SECOND MODEL, USING THE ENTIRE COHORT WAS
04 LOOKING AT THOSE PEOPLE WITH THE MOST EXPOSURE
05 INCORPORATED A FIVE-YEAR LAG MODEL, AND THAT -- IN THAT
06 REGRESSION, THEY ARE RELATIVELY UNIFORM -- THE UNIFORM
07 RELATIVE RISK, EXCEPTING THE PEOPLE WITH 15 TO 17 YEARS OF
08 EXPOSURE.
09 WE CAME TO FIND OUT THAT AGE GROUP, THAT
10 ESTIMATE IS QUITE UNSTABLE, DEPENDING -- NOT ONLY DOES IT
11 DEPEND ON THE FEW NUMBER EVENTS, AND A FEW CELLS, BECAUSE
12 WE'RE MISSING DEATHS, IT DEPENDS ON HOW YOU MODEL CALENDAR
13 YEAR AND AGE.
14 AND WHEN YOU TAKE THAT OUT, THE RELATIVE RISK
15 APPEARS TO BE MORE UNIFORM. AND THIS TAKES -- THIS IS
16 FOLLOW UP FOR 1976, BUT THIS IS WHAT ALLAN WAS REFERRING
17 TO. HE THOUGHT OUR FIRST ANALYSIS WAS PROPER.
18 WE'RE BACKING OFF FROM THAT SAYING THAT
19 ESTIMATE IS VERY UNSTABLE. AND TO REALLY GET AT
20 DOSE-RESPONSE, AT LEAST FROM YEARS OF EXPOSURE FROM '59,
21 WE NEED MORE YEARS OF FOLLOW UP.
22 NOW, WE'VE ALSO SAID THAT THE YEARS BEFORE
23 1959 IS IMPORTANT IN DETERMINING THIS DOSE-RESPONSE. AND
24 WE'VE NOT DONE THAT IN OUR PREVIOUS WORK BECAUSE OF
25 RELUCTANCE OF TRYING TO GUESS WHEN PEOPLE STARTED WORKING
0150
01 WITH DIESEL LOCOMOTIVES. THIS ANALYSIS, THIS SIMULATION
02 ATTEMPTS TO MODEL THAT UNCERTAINTY, AND IT COMES UP WITH A
03 RELATIVELY UNIFORM SLOPE.
04 DR. FROINES: BUT IF -- I THINK PAUL STILL HASN'T
05 GOT AN ANSWER.
06 DR. BLANC: NO, I GOT AN ANSWER. THE ANSWER WAS
07 THAT THE INITIAL ANALYSIS SHOWED THAT PEOPLE WHO STARTED
08 EARLIER HAD MORE RISKS THAN THE PEOPLE WHO HAD THE HIGHER
09 EXPOSURE JOBS THAN THE PEOPLE WHO HAD THE HIGHER EXPOSURE
10 JOBS, AND THE OTHER ANALYSIS HAD THE HIGHEST RISK.
11 DR. FROINES: I'M TRYING TO SEPARATE OUT WHAT --
12 DR. GARSHICK: THERE'S TWO ANALYSES.
13 DR. FROINES: -- IN FACT, CAN BE LEARNED FROM THE
14 DATA THAT WE HAVE, WHICH IS WHAT ALLAN DREW HIS
15 CONCLUSIONS, FROM AND WHAT DEPENDS UPON DOING FURTHER

16 RESEARCH. AS MUCH AS I RESPECT TOM SMITH AND ERIC, OF
17 COURSE THERE'S ROOM FOR MORE RESEARCH TO CHARACTERIZE
18 TO -- TO FURTHER CHARACTERIZE THESE QUESTIONS.
19 BUT WE'RE HERE IN THE BUSINESS OF TRYING TO
20 DECIDE WHAT IS IT WE KNOW ABOUT THESE DATA, WHAT DO THEY
21 TELL US GIVEN THE CIRCUMSTANCES WE FIND OURSELVES IN. AND
22 I THINK THAT'S WHAT ALLAN IS TRYING TO DO AND I THINK
23 THAT'S WHAT PAUL IS TRYING TO DO. AND I DON'T HAVE ANY
24 PROBLEM WITH LOOKING AT THE 15- TO 17-YEAR --
25 DR. GARSHICK: EXACTLY.

0151

01 DR. FROINES: -- ISSUES, BUT I WOULD ALSO ARGUE
02 THAT WE CAN PUT THAT IN ANOTHER BOX AND SAY, THAT'S WHAT
03 WE'LL DO LATER. BECAUSE IT'S NOT GERMANE TO WHAT WE HAVE
04 TO DECIDE HERE AS A BODY.
05 AND I THINK THAT'S WHY WE NEED -- WE NEED TO
06 FIND OUT WHAT THE DATA TELLS US THAT WE CAN THEN USE TO
07 DRAW CONCLUSIONS AND MAKE DECISIONS ABOUT.
08 DR. GARSHICK: YOU KNOW, AND JUST -- JUST FROM MY
09 PERSPECTIVE, THE DOSE-RESPONSE AS INITIALLY PUBLISHED IS
10 NOT QUITE AS CLEAR-CUT. THERE APPEARS TO BE A
11 DOSE-RESPONSE WHEN YOU LOOK AT AGE OF 59, BUT THE YEARS OF
12 EXPOSURE IS NOT AS CLEAR, AND THERE ARE LOTS OF REASONS
13 WHY THAT MAY BE -- MIGHT BE THE CASE.
14 DR. BLANC: CAN I ALSO ASK A QUICK QUESTION? I
15 DIDN'T GET A CHANCE TO THIS MORNING TO DR. MAUDERLY.
16 DR. FROINES: WELL, I THINK LET ALLAN FOLLOW UP AND
17 THEN YOU CAN GO BACK TO THAT.
18 DR. ALLAN SMITH: YES. I JUST WANT TO MAKE A POINT
19 THAT THERE'S A DANGER IN GOING BEYOND WHAT THE DATA
20 PERMIT. AND WHAT WORRIES ME ABOUT THAT COHORT -- AND I
21 AGREE. I MEAN, THERE SHOULD BE FURTHER WORK DONE ON IT.
22 IT WOULD BE NICE TO SEE FURTHER FOLLOW UP AND THINGS LIKE
23 THAT.
24 BUT THE QUESTION IS WHAT CAN BE INTERPRETED
25 ABOUT IT NOW, AND IN THAT REGARD, YOU'VE GOT THE

0152

01 ASSOCIATION YOU WOULD EXPECT TO FIND. THE YOUNGER PEOPLE
02 WHO HAD THE LONGER POTENTIAL FOR EXPOSURE HAD THE HIGH
03 RISK.
04 BUT AS SOON AS YOU THEN TRY AND TEASE OUT
05 AGE, CALENDAR TIME, AND LATENCY OF FOLLOW UP, FROM THAT
06 DATA SET, I THINK YOU GET INTO THE SITUATION WHERE YOU
07 JUST PRODUCE NONSENSE. AND I'M NOT BEING CRITICAL OF
08 BEING TRYING TO DO IT, BUT I DON'T THINK YOU CAN INTERPRET
09 MUCH BEYOND THOSE -- THAT -- THOSE INITIAL FINDINGS.
10 DR. FROINES: STAN?
11 DR. GLANTZ: YEAH, I MEAN, I AGREE WITH THAT. I
12 MEAN, I THINK THE -- YOU GET A HUGE MULTICOLLINEARITY
13 PROBLEM IN THE ANALYSIS WHEN YOU TRY TO PUT ALL THAT STUFF
14 IN AT THE SAME TIME. AND I THINK THAT'S WHY THE ESTIMATES
15 THAT YOU GET GET SO UNSTABLE WHEN YOU -- BECAUSE I THINK
16 YOU'RE OVER -- YOU KNOW, YOU'RE JUST PUTTING MORE INTO THE
17 MODEL THAN THE STATISTICS CAN SEPARATE OUT.
18 DR. FUCALORO: WE HAVE A KIND OF, IT SEEMS TO ME,
19 AN INTERESTING SITUATION HERE WHERE WE'RE GETTING SOME OF
20 THE ADVISE FROM THE PEOPLE HERE, INCLUDING DR. MACK AND

21 DR. ALLAN SMITH ABOUT -- WARNING NOT TO PLACE OVERRELIANCE
22 ON DOSE-RESPONSE CURVES, AND YET WE HAVE SOME PEOPLE HERE
23 WHO ARE WORKING VERY HARD TO GET DOSE-RESPONSE CURVES.
24 I WOULD LIKE TO -- I WOULD LIKE TO ASK
25 DR. TOM SMITH, WHAT DOES HE THINK OF THE ADVICE THAT WE
0153
01 SHOULDN'T OVERLY RELY UPON A DOSE-RESPONSE CURVES IN ORDER
02 TO MAKE THE DECISION WE NEED TO MAKE SOON?
03 DR. TOM SMITH: WELL, THAT'S -- I THINK, IN FACT,
04 THAT CUTS TO THE CENTER OF THE ISSUE. MY PERSONAL VIEW IS
05 THAT -- THAT THE DATA, AS SUMMARIZED BY ALLAN, WERE -- ARE
06 RATHER CONVINCING.
07 AND I THINK THAT THE QUESTION, DOES EXPOSURE
08 TO DIESEL EXHAUST IN A VARIETY OF CONTEXTS APPEAR TO
09 ELEVATE RISK OF LUNG CANCER? I THINK WE CAN ANSWER FAIRLY
10 COMFORTABLY, YES.
11 BUT THE NEXT QUESTION, ALL RIGHT, GIVEN A YES
12 TO THAT, HOW MUCH EXPOSURE CAUSES HOW MUCH RISK? I DON'T
13 THINK WE HAVE THE DATA TO ANSWER THAT QUESTION, AND THE
14 REASON WE DON'T HAVE THAT DATA IS BECAUSE WE'VE BEEN
15 TRYING TO ANSWER THE FIRST QUESTION.
16 AS A SCIENTIST WHOSE GOAL IN LIFE, IF YOU
17 WANT, IS TO DEFINE DOSE-RESPONSE RELATIONSHIPS USING
18 EPIDEMIOLOGIC TYPES OF DATA, THIS STUDY REPRESENTS THE
19 BEST WE COULD DO IN 1980. WE COULD DO MUCH, MUCH BETTER
20 NOW. AND KATHIE POINT OUT A LOT OF THE REASONS AND SO
21 FORTH, SO THAT I'M AFRAID THE BEST YOU CAN HOPE TO DO AT
22 THIS POINT IS DEFINE THAT THERE'S SOME VERY WIDE RANGE
23 THAT THE EXPOSURES MAY HAVE BEEN IN.
24 AND GIVEN THAT, IT'S UP TO THE POLICY SIDE OF
25 THE HOUSE, IF YOU WANT, TO DECIDE IF THAT'S SUFFICIENT TO
0154
01 MOVE AHEAD. AND I'M NOT A POLICY PERSON, SO I CAN'T
02 ANSWER THAT QUESTION. IN FACT, I SUSPECT YOU GUYS ARE
03 MUCH BETTER -- POSITION FOR THAT THAN ME.
04 DR. FROINES: WELL, I THINK, TOM, I THINK WHAT
05 YOU'VE JUST SAID IS VERY HELPFUL TO EVERYONE, AND I THINK
06 THAT -- THAT I THINK THE GROUP IN HERE WOULD PROBABLY BE
07 VERY HAPPY TO TURN OVER THOSE SUBSEQUENT DECISIONS OF RISK
08 MANAGEMENT BASED ON THE QUALITATIVE FINDINGS TO THE RISK
09 MANAGERS, AND WE SHOULD GIVE THEM HELP IN TRYING TO WORK
10 THAT OUT.
11 BUT -- BUT THE ACTUAL POLICY ISSUES ABOUT HOW
12 ONE THEN TAKES A BROAD RANGE OF RISK ESTIMATE AND THEN
13 USES IT FOR REGULATORY PURPOSES, FORTUNATELY, IS NOT THE
14 TASK OF THE PEOPLE SITTING IN THIS ROOM.
15 AND SO I THINK THAT WHAT YOU SAID, THOUGH, IS
16 VERY HELPFUL, AND I THINK THAT WE WILL -- I WOULD GUESS
17 THAT, IN FACT -- AND IT'S CONTAINED WITHIN THE DOCUMENT,
18 THAT THERE WILL BE A RANGE OF RISKS THAT'S REASONABLY WIDE
19 PRECISELY BECAUSE OF THAT.
20 DR. GLANTZ: WELL, I JUST WANT TO PICK UP ON THAT
21 WITH TWO POINTS. ONE, JUST FOR THE RECORD, I MEAN, IS
22 THERE ANYBODY HERE -- NOT HERE, BUT ANYBODY AROUND THIS
23 TABLE THAT WOULD -- I MEAN, I JUST WANT TO READ THE
24 DEFINITION -- THIS MAY AVOID A LOT OF FUTURE DISCUSSION.
25 THE DEFINITION OF A TOXIC AIR CONTAMINANT

0155

01 UNDER CALIFORNIA LAW IS AN AIR POLLUTANT WHICH MAY CAUSE
02 OR CONTRIBUTE TO AN INCREASE IN MORTALITY OR AN INCREASE
03 IN SERIOUS ILLNESS WHICH MAY POSE A PRESENT OR POTENTIAL
04 HAZARD TO HUMAN HEALTH.

05 I MEAN, IS THERE -- ARE ANY OF THE
06 SPEAKERS -- I MEAN, I GUESS THE PANEL SHOULDN'T DISCUSS
07 THIS, BUT IS THERE ANYBODY AMONG THE SPEAKERS WHO THINKS
08 THAT DIESEL DOES NOT MEET THAT DEFINITION? DIESEL EXHAUST
09 DOES NOT -- I MEAN, IS THERE ANYBODY AMONG THE SPEAKERS
10 WITHOUT ARGUING ABOUT DOSE-RESPONSE OR POTENCY, WHICH IS A
11 DIFFERENT QUESTION, WHO THINKS THAT -- THAT -- WHO WOULD
12 RECOMMEND TO THIS PANEL THAT DIESEL NOT BE DEFINED AS A --
13 DOES NOT MEET THE CRITERIA OF THE DEFINITION OF A TOXIC
14 AIR CONTAMINANT UNDER CALIFORNIA LAW?

15 DR. FROINES: I THINK YOU GOT SILENCE THE FIRST
16 TIME --

17 DR. GLANTZ: OKAY.

18 DR. FROINES: AND WITH THAT --

19 DR. GLANTZ: OKAY. I JUST WANTED TO BE SURE NO ONE
20 FELL ASLEEP.

21 FELL DR- FROINES: WITH ACADEMICS, YOU ASK THE
22 QUESTION TWICE, YOU'LL GET SOMEBODY POPPING IN. SO GO
23 WITH THE FIRST SILENCE.

24 DR. GLANTZ: OKAY. AND THEN I WILL GO ON.

25 I WANT TO JUST DISAGREE WITH SOMETHING YOU

0156

01 SAID, JOHN, AND THAT IS, I MEAN, I THINK WE DO HAVE AN
02 OBLIGATION TO TRY -- WELL, WE ARE NOT INVOLVED IN THE RISK
03 MANAGEMENT PHASE OF THIS PROCESS. I MEAN, I THINK WE DO
04 HAVE AN OBLIGATION TO DO THE BEST WE CAN TO TELL PEOPLE,
05 YOU KNOW, WHAT WE THINK THE POTENCY OF THIS IS AND GIVE
06 THEM SOME GUIDANCE AS TO WHAT WE THINK THE BEST AVAILABLE
07 INFORMATION IS.

08 AND SO, I MEAN, I THINK THAT THE ALL OF THE
09 DISCUSSION THAT SEVERAL PEOPLE HAVE MADE ABOUT THE NEED
10 FOR FUTURE RESEARCH, AND THE FACT THAT WE DON'T KNOW
11 EVERYTHING. I MEAN, THIS IS A MANTRA WE GO THROUGH ON
12 EVERY SINGLE COMPOUND THAT COMES BEFORE US. WE WISH WE
13 KNEW MORE, WE WISH WE KNEW MORE.

14 BUT I MEAN, I THINK DR. GARSHICK RAISED A
15 REAL INTERESTING POINT WITH THIS BLUE SLIDE I WAS JUMPING
16 ALL OVER BECAUSE IT MAY BE THAT BY USING THE LINEAR
17 DOSE-RESPONSE ASSUMPTION WITH EXPOSURE, WE'RE GROSSLY
18 UNDERESTIMATING THE POTENCY, AND MAYBE WE OUGHT TO BE
19 USING SOMETHING LIKE THAN WHAT HE SUGGESTED, WHICH WOULD
20 BE A MUCH HIGHER POTENCY.

21 DR. GARSHICK: WELL, I DIDN'T SUGGEST A MODEL.

22 DR. GLANTZ: OH, WELL, NO. I WAS JUST TALKING
23 ABOUT THE DATA THERE. I CAN DRAW THE LINE THROUGH IT.

24 DR. GARSHICK: I THINK WE HAVE TO KNOW SOMETHING
25 ABOUT THE BIOLOGY, THOUGH, I MEAN, OF WHAT'S GOING ON.

0157

01 DR. GLANTZ: WELL --

02 DR. FROINES: ANYWAY, THE TWO OF YOU HAVE HAD THIS
03 DISCUSSION AT LEAST THREE TIMES.

04 DR. GLANTZ: OKAY. WELL, THEY WERE ACADEMIC.

05 DR. FROINES: I REMEMBERED IT. I REMEMBERED IT THE
06 FIRST TIME, THE SECOND TIME, AND THE THIRD TIME, AND NOW
07 I'M GOING TO CLOSE IT OFF FOR SAKE OF LUNCH.
08 DR. BLANC: JOHN, JOHN, COULD I --
09 DR. FROINES: I THINK THAT THE ISSUE YOU'RE RAISING
10 IS REALLY QUITE CRUCIAL, AND CLEARLY THIS IS A DISCUSSION
11 THAT HAS TO OCCUR AMONG THE PANEL IN APRIL WHEN WE TAKE
12 THE DOCUMENT UP IN ITS ENTIRETY.
13 BUT SO I THINK GETTING AS MUCH INFORMATION
14 FROM THIS GROUP OF PANEL AND OTHERS IS GOING TO HELP US BE
15 ABLE TO DO THAT. AND SO THE -- AND SO YOUR QUESTION TO
16 THE PANEL IS HIGHLY RELEVANT.
17 AND SOMEBODY WAS TRYING TO GET MY ATTENTION?
18 DR. BLANC: I WAS BECAUSE I STILL WANTED TO ASK THE
19 QUESTION --
20 DR. FROINES: OH, I'M SORRY.
21 DR. BLANC: -- TO DR. MAUDERLY.
22 ACTUALLY, TWO SMALL QUESTIONS. ONE HAS TO DO
23 WITH YOUR COMMENT ON THE CARCINOGENIC RESPONSE IN --
24 DESCRIBES SUSCEPTIBLE STRAINS OF MICE.
25 DO YOU HAVE ANY DATA ON WHETHER THOSE
0158
01 SUSCEPTIBLE STRAINS OF MICE SIMILARLY RESPOND TO TITANIUM
02 DIOXIDE OR CARBON BLACK, OR IS THEIR RESPONSE TO DIESEL
03 DIFFERENT THAN THEIR RESPONSE TO NONSPECIFIC OR INERT
04 PARTICULATE?
05 DR. MAUDERLY: I DON'T RECALL ANY STUDIES THAT HAVE
06 BEEN CONDUCTED WITH THOSE STRAINS WITH TITANIUM DIOXIDE OR
07 CARBON BLACK. NOW, I GUESS THAT'S NOT A CERTAINTY IF
08 THERE HASN'T BEEN A STUDY, BUT I'M FAMILIAR WITH THE
09 LITERATURE. I'M NOT AWARE THAT'S BEEN DONE. AND SO I
10 CAN'T ANSWER THAT QUESTION.
11 DR. BLANC: SO YOU DON'T HAVE ANY REASON TO BELIEVE
12 A PRIORI THAT THE RESPONSE OF THOSE SUSCEPTIBLE
13 SPECIES -- SUSCEPTIBLE STRAINS OF MICE, ALTHOUGH SOMEWHAT
14 VARIABLE IN WHAT PEOPLE HAVE FOUND REPRESENTS THE SAME
15 MECHANISM THAT YOU ARE DESCRIBING IN RATS, THAT THOSE
16 SUSCEPTIBLE STRAINS ARE SUSCEPTIBLE BECAUSE THEY BEHAVE
17 LIKE RATS.
18 YOU DON'T HAVE ANY REASON, ANY PRIORI TO
19 BELIEVE THAT?
20 DR. MAUDERLY: NO. I REALLY HAVE NO INFORMATION ON
21 WHICH TO -- TO MAKE AN INTELLIGENT GUESS ONE WAY OR THE
22 OTHER.
23 DR. BLANC: OKAY. AND SECOND QUESTION IS IN TERMS
24 OF THE RAT RESPONSE IN THE LOWER END OF THE RANGE AT WHICH
25 THE RATS RESPOND TO DIESEL, AND IN TERMS OF CUMULATIVE
0159
01 DOSE -- AND I DON'T REMEMBER THE EXACT SCALE, BUT LET'S
02 TAKE THAT LOWISH END BEYOND THE AREA IN WHICH YOU --
03 YOU'RE EYEBALLING FELT THAT THERE WASN'T A RESPONSE, BUT
04 NOT AT THE FAR RIGHT HAND.
05 IS THAT A CUMULATIVE DOSE-RESPONSE AREA IN
06 WHICH THERE'S ALSO A RESPONSE IN YOUR HANDS WITH TITANIUM
07 DIOXIDE AND CARBON BLACK? OR HAVE YOUR EXPOSURES TO
08 CARBON BLACK AND TITANIUM DIOXIDE IN TERMS OF CUMULATIVE
09 EXPOSURE BEEN MORE AT THE FAR RIGHT END OF THAT SCALE?

10 DR. MAUDERLY: ALL OF OUR WORK -- WE HAVE NOT
11 WORKED WITH TITANIUM DIOXIDE. OTHERS HAVE. WE HAVE
12 WORKED WITH CARBON BLACK. ALL OF OUR CARBON BLACK WORK HAS
13 BEEN UP AT THE HIGH DOSE END.
14 DR. BLANC: THE FAR END?
15 DR. MAUDERLY: YES. AND I'M TRYING TO RECALL. I
16 CANNOT RECALL THAT THERE HAS BEEN TITANIUM DIOXIDE OR
17 CARBON BLACK WORK DOWN IN THAT SORT OF LOW DOSE OR
18 INTERMEDIATE DOSE --
19 DR. BLANC: IN THE INTERMEDIARY DOSE?
20 DR. MAUDERLY: I WOULD HAVE TO GO BACK TO THE
21 STUDIES TO LOOK TO BE CONFIDENT IN SAYING THAT THAT'S NOT
22 THE CASE, BUT -- BUT THOSE STUDIES HAVE GENERALLY BEEN IN
23 HIGH DOSE REGIMES.
24 DR. BLANC: IN VERY HIGH DOSE?
25 DR. MAUDERLY: UH-HUH.

0160
01 DR. BLANCK: SO IT WOULD BE ONE POSSIBLE -- TO
02 FOLLOW UP TO THAT, ONE POSSIBLE CONSERVATIVE WAY OF
03 LOOKING AT THE RAT DATA MIGHT BE WITH THE DIESEL TO, LET'S
04 SAY, ELIMINATE THE DOSES IN THE -- CUMULATIVE DOSES IN THE
05 RANGE WHERE THERE IS A NONSPECIFIC EFFECT, AND LOOK AT
06 SOME OF THE INTERMEDIATE AND LOW DOSES AND SEE WHAT ONE'S
07 DOSE-RESPONSE LOOKED LIKE IN THAT WAY, POTENTIALLY?
08 DR. MAUDERLY: WELL, IF I INTERPRET YOUR QUESTION
09 CORRECTLY, YOU'RE GETTING THE AT THE ISSUE OF WHETHER OR
10 NOT THERE'S A PORTION OF THAT POSITIVE DOSE-RESPONSE CURVE
11 THAT MIGHT BE RELEVANT IF WE CUT OFF SOME OTHER PORTION?
12 DR. BLANC: THAT'S CORRECT.
13 DR. MAUDERLY: BIOLOGICALLY -- AND I DON'T KNOW
14 ANSWER TO THAT STATISTICALLY. I MEAN THAT I SUPPOSE ONE
15 COULD DO --
16 DR. BLANC: I'M ASKING YOU BIOLOGICALLY, AND THAT'S
17 ALL.
18 DR. MAUDERLY: BIOLOGICALLY, WHAT WE SEE IN THESE
19 STUDIES IS THAT WE DO NOT SEE A TUMOR RESPONSE IN ANY
20 STUDY THAT I'M AWARE OF WITH THESE KINDS OF PARTICLES IN
21 WHICH THERE IS NOT ALSO A -- WHAT HAS COMMONLY BEEN TERMED
22 OVERLOADING, WHICH IS A VERY POOR NONSPECIFIC TERM. BUT
23 AN ACCUMULATION OF PARTICLES, AN OVERWHELMING OF
24 CLEARANCE, A PERSISTENT INFLAMMATION AND CELL
25 PROLIFERATIVE AND FIBROTIC DISEASE, AND SO I DO NOT SEE

0161
01 THE EARLY PARTS OF THAT POSITIVE SLOPE AS REPRESENTING
02 DIFFERENT MECHANISMS THAN THIS -- THAN THE HIGHER DOSE
03 PARTS.
04 DR. BLANC: BUT ACTUALLY, THE STUDIES HAVE NOT BEEN
05 DONE WITH THE INERT PARTICLES AT THOSE KIND OF CUMULATIVE
06 LEVELS FROM WHAT YOU'RE SAYING? EITHER IN YOUR HANDS OR
07 ANYONE ELSE'S BECAUSE THE CARBON BLACK AND THE TITANIUM
08 HAVE BEEN AT THE VERY HIGH END? IS THAT --
09 DR. MAUDERLY: YES, YES.
10 DR. BLANC: IS THAT WHAT I UNDERSTAND -- OKAY.
11 THANKS.
12 DR. MAUDERLY: AND YOUR POINT IS WELL-TAKEN, THAT
13 IT WOULD BE INTERESTING TO KNOW WHAT SOME OF THOSE OTHER
14 PARTICLES WITHOUT MUTAGENS DID DOWN IN THAT SORT OF

15 BORDERLINE AREA. AND AGAIN, THERE MAY BE STUDIES. I'M
16 NOT RECALLING. BUT I'M REASONABLY CONFIDENT IN SAYING
17 THAT WE JUST DON'T KNOW THAT ANSWER TODAY.
18 DR. FROINES: THERE ARE A NUMBER -- THIS RAISES A
19 NUMBER OF QUESTIONS, BUT I THINK WE HAVE TO -- MAYBE I'LL
20 COME BACK TO IT LATER.
21 TOM, DID YOU WANT TO SAY SOMETHING?
22 DR. MACK: NO.
23 DR. FROINES: NO. KATHIE, THEN.
24 DR. HAMMOND: JUST A QUICK COMMENT. I THOUGHT THAT
25 THERE WAS -- JOE, THAT YOU HAD A VERY INTERESTING SLIDE
0162
01 THAT SHOWED THE RESULTS FOR CHEMICALS WHICH WERE
02 CARCINOGENIC IN RATS AND NOT IN MICE. AND I THINK IT'S
03 IMPORTANT FOR PANEL TO REMEMBER THAT THAT INCLUDED MANY
04 KNOWN HUMAN CARCINOGENS. SO THERE'S EVIDENCE ALREADY OF
05 HUMAN CARCINOGENS THAT ARE CARCINOGENIC IN RATS, NOT IN
06 MICE. SO WE REALLY CAN'T DEDUCE, YOU KNOW, THE LACK OF
07 CARCINOGENICITY OF DIESEL EXHAUST IN MICE TELLS US
08 ANYTHING.
09 DR. FROINES: I -- AND WELL, IN THAT REGARD --
10 DR. HAMMOND: AND THAT INCLUDED SILICA, CADMIUM,
11 NICKEL.
12 DR. FROINES: JOE MAY WANT TO RESPOND TO THAT.
13 BUT THERE WAS A GOOD PAPER IN A.J.I.M. LAST
14 YEAR BY JACK SIMIATICKI (PHONETIC) IN WHICH HE DID A HUMAN
15 STUDY, AND IT WAS A PRETTY SOLID PIECE OF WORK.
16 AND HE SEEMED TO INDICATE THAT THERE WAS
17 CONSIDERABLE EVIDENCE FOR CANCER IN CARBON WORKERS.
18 AND THE QUESTION IS HOW DO YOU INTERPRET
19 CANCER IN CARBON BLACK WORKERS GIVEN THE -- GIVEN THE
20 ASSUMPTION THAT THEY SHOULDN'T BE GETTING CANCER IN
21 HUMANS, AND APPARENTLY DO.
22 DR. MAUDERLY: WELL, LET ME -- LET ME TRY TO
23 RESPOND TO BOTH OF THOSE AS BEST I CAN.
24 I -- I WOULD AGREE THAT A PRIORI THE ABSENCE
25 OF A POSITIVE RESPONSE IN MICE, AND THE PRESENCE OF A
0163
01 POSITIVE RESPONSE IN RATS DOES NOT NECESSARILY MEAN THAT
02 IT'S NOT A HUMAN CARCINOGEN.
03 YOU KNOW, WE ARE DEALING FROM A BIOLOGICAL
04 STAND POINT. WE'RE DEALING WITH WHAT SEEMS TO BE A
05 SPECIES UNIQUE RESPONSE, OR AT LEAST OF THE SPECIES THAT
06 HAVE BEEN TESTED SO FAR, TO HEAVY PARTICLE LOADINGS.
07 AND MY USE OF THAT SLIDE WAS TO ILLUSTRATE
08 THAT THIS IS NOT AN ISSUE THAT IS JUST RAISED BY DIESEL
09 SOOT, BUT BY MANY OTHER PARTICLES.
10 BUT THAT -- YOU KNOW, I WOULD AGREE WITH YOU
11 THAT THAT IN ITSELF DOES NOT CONFIRM IT IN ANY WAY, DOES
12 NOT PROVE THAT IT'S NOT A HUMAN CARCINOGEN.
13 NOW, REGARDING THE CARBON BLACK STUDIES
14 HAVING JUST HEARD THOSE REVIEWED ONCE AGAIN LAST FRIDAY AT
15 THE A.C.G.I.H. MEETING, I THINK THE JURY IS STILL OUT AS
16 TO WHETHER THERE IS A -- ANY KIND OF CONSISTENT SIGNAL
17 FROM THE CARBON BLACK STUDIES. THERE ARE CERTAINLY SOME
18 STUDIES THAT HAVE GIVEN POSITIVE RESULTS, AND THIS SOUNDS
19 LIKE A VERY FAMILIAR STORY.

20 THERE ARE ALSO SOME STUDIES THAT DON'T GIVE
21 POSITIVE RESULTS. AND I DON'T HAVE AN ANSWER FOR THAT AT
22 THIS POINT.

23 THERE ARE MANY DIFFERENT KINDS OF CARBON
24 BLACKS. SOME OF THEM DO HAVE ORGANIC CONTENT AND OTHERS
25 DON'T. THE ONES THAT WERE CHOSEN FOR THE RAT STUDIES, THE
0164 TWO THAT I PORTRAYED, ALTHOUGH THEY WERE DIFFERENT CARBON
01 BLACKS, THEY WERE BOTH SELECTED BECAUSE THEY HAD VIRTUALLY
02 NO IMMUTAGENIC ACTIVITY.

03 WHETHER THAT REPRESENTS ALL KINDS OF CARBON
04 BLACK EXPOSURES, I CAN'T SPEAK TO THAT ISSUE.

05 DR. ZIELINSKA: I JUST WANTED TO MAKE A QUICK
06 COMMENT. IT DOESN'T NECESSARILY MEAN THAT CARBON BLACK
07 NOT -- DOESN'T CONTAIN ANY ORGANICS. ACTUALLY, WE WERE
08 ANALYZING SOME OF THIS WHICH WERE USED FOR FUTURE -- FOR
09 THE FUTURE ANIMAL STUDY, AND WE FOUND CONCENTRATION OF
10 P.A.H.'S QUITE SIGNIFICANT.

11 DR. MAUDERLY: OH, YES. I WOULD AGREE WITH THAT.
12 I MEAN, AND THERE'S -- THERE ARE A LARGE NUMBER OF CARBON
13 BLACKS, AND THEY HAVE VARIABLE AMOUNTS OF ORGANIC CONTENT,
14 AND SOME OF THEM ARE QUITE HIGH. I WOULD NOT DISAGREE
15 WITH THAT.

16 DR. FROINES: I'M GETTING ALL THESE NOTES HERE
17 SAYING WE HAVE TO STOP FOR LUNCH BECAUSE THERE'S A CUTOFF
18 FOR LUNCH.

19 BUT I THINK THE OTHER QUESTION IS WHEN YOU
20 ARE EXPOSED TO THINGS THAT ARE POTENT MUTAGENS, THEN THE
21 QUESTION THEN BECOMES AS A BIOLOGICAL MATTER, WHY DON'T
22 YOU SEE CANCERS BY THAT MECHANISM?

23 AND IT SEEMS TO ME THAT IT'S ONE THING TO
24 ASSERT THAT IT ONLY OCCURS WITH OVERLOAD BUT -- BUT THE
0165 EXPLANATION OF IF YOU'RE EXPOSED TO P.A.H.'S AND
01 NITRO-P.A.H.'S AND WHOLE SUBUTADINE (PHONETIC) AND THE
02 WHOLE SERIES OF COMPOUND THAT YOU WOULD NORMALLY EXPECT TO
03 HAVE PRODUCE CANCER, YOU'RE ARGUING THAT IN THE RAT, THOSE
04 CANCERS ARE NOT PRODUCED FROM THOSE CARCINOGENS.

05 AND IT SEEMS TO ME WE HAVE TO HAVE AN
06 EXPLANATION FOR THAT, NOT SIMPLY JUST TO ASSUME THAT NONE
07 OF THAT IS OPERABLE.

08 DR. MAUDERLY: WELL, MY ONLY RESPONSE TO THAT CAN
09 BE THAT WHAT I'VE DONE TO PORTRAY THE EVIDENCE WE HAVE,
10 AND THE EVIDENCE WE HAVE SUGGESTS THAT IF THERE IS
11 ACTIVITY FROM THOSE MATERIALS IN THESE TWO COMPARATIVE
12 STUDIES, IT'S NOT APPARENT.

13 DR. FROINES: I'M SORRY. THAT WAS A BAD
14 BEFORE-LUNCH QUESTION, AND IT'S OBVIOUSLY GOING TO TAKE A
15 LOT LONGER DISCUSSION.

16 SO BILL LOCKETT HAD AN ANNOUNCEMENT TO MAKE
17 ABOUT LUNCH.

18 MR. LOCKETT: WHAT TIME ARE WE RECONVENING?

19 DR. FROINES: 2:00.

20 MR. LOCKETT: ONE OPTION FOR LUNCH IS TO EAT HERE
21 AT THE LOWER LEVEL, WHICH IS THE BASEMENT. TO DO SO,
22 THOUGH, YOU NEED TO BUY A LUNCH TICKET AT THE FIRST FLOOR
23 COUNTER. THAT'S 6.50 PLUS TAX. THE FIRST FLOOR ALSO HAS
24

25 OTHER OPTIONS. IF YOU WANT TO GO ELSEWHERE FOR LUNCH --
0166
01 SO IF YOU DECIDE TO GET YOUR TICKET, AFTER YOU'VE HAD YOUR
02 TICKET, THEN PROCEED TO THE LOWER LEVEL OF THE CAFETERIA
03 AND THERE IS KIND OF A LARGE SELECTION OF CHANGES FOR
04 FOOD. BON APETITE.
05 DR. FROINES: THANK YOU, EVERYONE. THIS HAS GONE
06 VERY, VERY SMOOTHLY AND WELL. AND I THINK THE INFORMATION
07 HAS BEEN VERY VALUABLE. SO HOPEFULLY WE CAN CONTINUE IN
08 THE AFTERNOON.
09 (LUNCH)
10 DR. FROINES: EVERYBODY READY? WE WANT THE WORLD
11 TO KNOW THAT THIS IS A DISCIPLINED, WELL-ORGANIZED GROUP.
12 AND, STAN, YOU'RE OUR MODEL.
13 DR. GLANTZ: WHAT AM I? A MODEL OF WHAT?
14 DR. FROINES: DISCIPLINE AND ORGANIZATION.
15 DR. GLANTZ: I'M NOT EVEN WEARING A TIE.
16 DR. FROINES: WELL, I KNOW. I WAS GOING TO SPEAK
17 TO YOU ABOUT THAT AFTERWARDS.
18 WE ARE ANTICIPATING TO HAVE OUR FIRST SPEAKER
19 OF THE AFTERNOON BE DR. KENNETH CRUMP, AND I WON'T GO INTO
20 THAT BECAUSE WE'VE ALL BEEN AWARE OF THE CRUMP/DAWSON
21 DEBATE AS IT WERE, AND SO --
22 DR. GLANTZ: THAT'S A MINI-SERIES, ISN'T IT?
23 DR. FROINES: IT'S GOING TO REPLACE SEINFELD.
24 BUT I'M VERY PLEASED TO HAVE DUNCAN THOMAS
25 START OUT THE AFTERNOON. I -- I DIDN'T FOR A MINUTE
0167
01 ANTICIPATE THAT HE WOULD BE WILLING TO DO IT, BUT HE
02 AGREED, AND WE ARE ALL GOING TO BE THE BETTER OF IT.
03 SO DUNCAN IS AT U.S.C. HE'S PART OF THE
04 SOUTHERN CALIFORNIA ENVIRONMENTAL HEALTH SCIENCES CENTER.
05 HE'S A STATISTICIAN OF NOTE AND DUNCAN THOMAS.
06 DR. THOMAS: I THINK I'M HERE BECAUSE I WAS RASH
07 ENOUGH TO TAKE POT SHOTS AT THE 1994 DRAFT OF THIS THING,
08 AND PEOPLE HAVE BEEN BUGGING ME EVER SINCE TO EXPLAIN
09 MYSELF. AND UP UNTIL THIS MOMENT, I'VE SUCCESSFULLY
10 RESISTED ALL OF THESE REQUESTS, BUT I FIGURE IT'S FINALLY
11 PUT UP OR SHUT UP TIME FOR ME.
12 SO WHAT I THINK I CAN PROBABLY CONTRIBUTE
13 BEST TO THIS DISCUSSION IS TO TRY TO SHED SOME LIGHT ON
14 THE CRUMP AND DAWSON DEBATE. AT LEAST THAT WAS MY HOPE
15 WHEN JOHN TWISTED MY ARM INTO -- INTO COMING HERE.
16 SINCE THEN I HAVE WADED THROUGH THIS DOCUMENT
17 AS ALL OF YOU, I SUSPECT MANY TIMES MORE THAN ME, AND
18 GOTTEN EVEN MORE CONFUSED THAN I WAS IN 1994.
19 AND SINCE WRITING UP SOME COMMENTS THAT I
20 THINK ARE BEING COPIED AND CIRCULATED FOR YOU, I HAVE BEEN
21 FURTHER INUNDATED WITH COMMENTS AND FURTHER CONTRIBUTIONS
22 FROM BOTH KENNY AND STAN, AND NOW EVEN MORE CONFUSED THAN
23 I WAS BEFORE. BUT LET ME DO THE BEST I CAN.
24 TO BEGIN WITH, LET ME JUST DISPENSE WITH THE
25 ISSUES THAT WERE DISCUSSED THIS MORNING, AND GO ON RECORD
0168
01 THAT SAYING THAT MY OVERALL VIEWS ABOUT THE
02 CARCINOGENICITY OF THE DIESEL EMISSIONS HASN'T CHANGED
03 SUBSTANTIALLY FROM THE COMMENTS I MADE IN 1994, AND WERE

04 ECHOED BY MANY OF THE PANELISTS THIS MORNING.
05 IF ANYTHING, THIS REDRAFT HAS MOVED THAT
06 SUPPORT FOR THE POSITION THAT DIESEL EXHAUSTS IS A HUMAN
07 CARCINOGEN ALONG CONSIDERABLY, AND THE ADDITION OF THE --
08 I THINK OUTSTANDING JOB OF A META-ANALYSIS TO THE DRAFT
09 THAT I'M NOW SEEING FOR THE FIRST TIME IS A SUBSTANTIAL
10 IMPROVEMENT, AND I FIND THAT QUITE CONVINCING.
11 THE OTHER THING WHICH THE ADDITION OF THAT
12 META-ANALYSIS ACCOMPLISHES IS THAT IT PROVIDES A SUMMARY
13 OF THE HUMAN RISKS BASED NOT, JUST ON THE GARSHICK
14 STUDIES, WHICH I AGREE WITH THE STATE IS STILL THE BEST
15 BASIS FOR QUANTITATIVE RISK ASSESSMENT, BUT OUR CONFIDENCE
16 IN THAT ASSESSMENT GOES FAR -- IS CONSIDERABLY IMPROVED BY
17 THE INCLUSION OF THE SUMMARY META-ANALYSIS WHICH WOULD
18 SUGGEST A RISK -- RELATIVE RISK TO SOMETHING OF THE ORDER
19 OF 1.3, 1.5, AND SIMPLE BACK OF THE ENVELOPE CALCULATIONS,
20 AS WERE INCLUDED IN THE DRAFT WHICH I FIRST REACTED TO
21 FOUR YEARS AGO, AND AS ILLUSTRATED BY ALLAN THIS MORNING,
22 ARE SUFFICIENT IN MY MIND TO PROVE THAT THE --
23 QUANTITATIVELY THE RISKS ASSOCIATED WITH GENERAL
24 POPULATION EXPOSURES TO DIESEL EMISSIONS ARE NONTRIVIAL.
25 SO HAVING -- EVEN IF WE WERE PREPARED TO
0169 REACH A CONCLUSION THAT DIESEL EMISSIONS OVERALL ARE HUMAN
01 CARCINOGENS, AND THEREFORE THE COMMITTEE SHOULD COME DOWN
02 ON THE SIDE OF SUCH A CONCLUSION, WE ARE STILL LEFT WITH
03 THE RISK ASSESSMENT PROBLEM.
04 AND THE ADDITION OF THIS SUMMARY
05 META-ANALYSIS NOW GIVES US ONE MORE WAY TO GO ABOUT THAT
06 AND REACH THE CONCLUSION THAT WE ARE LOOKING AT RATHER
07 NONTRIVIAL PROBLEM.
08 NOW, HOW CAN WE GO ABOUT DOING THIS
09 QUANTITATIVE RISK ANALYSIS AS WELL AS POSSIBLE? I DON'T
10 THINK BACK OF THE ENVELOPE CALCULATIONS CUT IT, ALTHOUGH
11 GIVEN THE LIMITATIONS OF THE PRIMARY EPIDEMIOLOGIC DATA
12 THAT WE HAVE TO WORK WITH, WE MAY NOT BE ABLE TO DO A
13 WHOLE LOT BETTER BY DOING WHAT WOULD BE THE STATE OF THE
14 ART RISK ASSESSMENT.
15 NOW, I FOUND FAULT WITH THE 1994 DRAFT'S
16 QUANTITATIVE RISK ASSESSMENT IN TWO BROAD AREAS.
17 THE FIRST WAS THE WAY THEY ARRIVED AT A
18 SUMMARY OF THE EPIDEMIOLOGIC SLOPE ESTIMATES, WHICH WOULD
19 GO INTO THE RISK CALCULATION; AND SECOND, IS HOW THEY USED
20 THAT SLOPE ESTIMATE THEN TO ARRIVE AT WHAT IS KNOWN AS A
21 UNIT RISK ESTIMATE.
22 AND I OUTLINED A STRATEGY THEN WHICH I
23 THOUGHT WAS MUCH BETTER, BUT WOULD REQUIRE GOING BACK TO
24 THE RAW DATA TO FIT THE MODEL OF CHOICE DIRECTLY TO THE
0170 ORIGINAL DATA TO DEVELOP AN EXPOSURE TIME RESPONSE
01 RELATIONSHIP OR -- AND THEN USE THAT EXPOSURE TIME
02 RESPONSE RELATIONSHIP IN A STANDARD LIFE TABLE KIND OF
03 CALCULATION TO ARRIVE AT AN ESTIMATE OF LIFETIME RISK.
04 AND I'M PLEASED TO SEE THAT THIS DRAFT HAS
05 INCORPORATED BOTH OF THOSE SUGGESTIONS. WE NOW HAVE A
06 QUITE EXTENSIVE BODY OF REANALYSES OF THE ORIGINAL
07 GARSHICK DATA WITH A WIDE VARIETY OF MODELS, WHICH AS WE

09 WILL SEE, LEAD TO SOMEWHAT CONFLICTING CONCLUSIONS IN THE
10 HANDS OF DIFFERENT DATA ANALYSTS; BUT ANYWAY, WE ARE
11 PRESENTED WITH QUITE A BROAD RANGE OF CHOICES ABOUT A
12 VARIETY OF DIFFERENT MODELING ASSUMPTIONS.

13 AND THEN IN THE SECOND STAGE, THE RESULTING
14 MODELS ARE USED EXPLICITLY IN AN APPROPRIATE LIFE TABLE
15 CALCULATION TO DERIVE A LIFETIME RISK ESTIMATE WHICH
16 RECOGNIZES THE FACT THAT CUMULATIVE EXPOSURE IS, BY
17 DEFINITION, NOT CONSTANT OVER A LIFETIME. CUMULATIVE
18 EXPOSURE ACCUMULATES; AND THEREFORE, THE RELATIVE RISK
19 CHANGES OVER LIFETIME, AND YOU CAN'T JUST SIMPLY, IF YOU
20 WANT THE RIGHT ANSWER, MULTIPLY THE AVERAGE LIFETIME RISK
21 IN THE GENERAL POPULATION BY A SUMMARY OF RELATIVE RISK
22 AND HOPE TO GET THE RIGHT ANSWER.

23 AND LIFE TABLE METHODS ARE IN PRINCIPAL THE
24 RIGHT WAY TO GO ABOUT IT.

25 NOW, THE MAJOR UNCERTAINTY WE HAVE IS HAVE WE
0171 GOT THE RIGHT DOSE-RESPONSE RELATIONSHIP. NOW, THIS TURNS
01 OUT TO BE A VERY COMPLICATED PROBLEM AND IS THE CORE OF
02 THE CRUMP/DAWSON DEBATE.

03 NOW, THERE ARE MANY, MANY DIFFERENCES BETWEEN
04 THE WAY THE TWO -- THESE TWO ANALYSTS AND THE ORIGINAL
05 ANALYSTS HAVE APPROACHED THE ANALYSIS. AND THERE ARE
06 THREE LENGTHY DIFFICULT, I SUSPECT TO MANY OF YOU,
07 VIRTUALLY INCOMPREHENSIBLE APPENDICES, AND CHAPTER 7
08 ITSELF IS TOUGH GOING EVEN IF YOU DON'T ATTEMPT THE
09 APPENDICES.

10 IF I HAD ONLY ONE REQUEST TO MAKE, IT WOULD
11 BE THAT SOMEBODY SEE IF THEY COULD TAKE THE MATERIAL
12 THAT'S IN CHAPTER 7 AND THE THREE SUPPORTING APPENDICES
13 AND TURN IT INTO ENGLISH. BUT I'M NOT VOLUNTEERING FOR
14 THAT JOB, AND I DON'T THINK THERE ARE VERY MANY PEOPLE
15 THAT HAVE BOTH THE EXPERTISE AND THE WILLINGNESS THAT
16 WOULD ACTUALLY BE ABLE TO PULL THIS OFF. SO I DON'T KNOW
17 HOW THE STATE IS GOING TO ACCOMPLISH THAT WISH, BUT I'M
18 HERE NOW TO TRY TO ELUCIDATE WHAT I SEE AS THE BASIC --
19 THE BIG PICTURE ISSUES.

20 APPENDIX -- I THINK IT'S APPENDIX D, IF I'M
21 NOT MISTAKEN, D OR E, OUTLINES IN SUMMARY FORM THE MAJOR
22 POINTS OF DIFFERENCE BETWEEN THE DIFFERENT ANALYSES.

23 AND THEN ONE OF THE OTHER APPENDICES, I THINK
24 IT'S APPENDIX E, THEN GOES ON TO PROVIDE SOME QUANTITATIVE
0172 RESULTS ABOUT THE IMPLICATION OF DIFFERENT MODELING
01 ASSUMPTIONS.

02 SOME THE ISSUES ARE TRIVIAL, SOME OF THE
03 ISSUES ARE MAJOR. AND IN MY WRITTEN COMMENTS, I HAVE
04 TRIED TO DISPENSE WITH WHAT I THINK ARE THE TRIVIAL
05 ISSUES. I STILL REMAIN TO BE EDUCATED BY PEOPLE THAT KNOW
06 THESE DATA BETTER THAN ME. SOME OF THE THING I THINK ARE
07 TRIVIAL ISSUE MAY NOT BE TRIVIAL, BUT I WANT TO FOCUS ON
08 THE TWO THAT I THINK ARE THE MAJOR ISSUES.

09 AND THE FIRST IS HOW WE GO ABOUT DEALING WITH
10 THE POTENTIALLY CONFOUNDING EFFECTS OF THE OTHER
11 TIME-RELATED VARIABLES LIKE ATTAINED AGE, AGED EXPOSURE,
12 CALENDAR YEAR, BIRTH COHORT.

14 AND THE SECOND IS THE ISSUE OF HOW WE ADDRESS
15 THE QUESTION OF BACKGROUND EXPOSURES. NOW, WHEN I WROTE
16 MY 1994 CRITIQUE OF THE FIRST OF THESE ISSUES, THE
17 CONFOUNDING EFFECT OF AGE, ET CETERA, LOOM VERY LARGE IN
18 MY THINKING.

19 I WAS UNHAPPY WITH THE WAY THE DATA HAD BEEN
20 ANALYZED ORIGINALLY, USING COX REGRESSION TECHNIQUES WHICH
21 TOOK CALENDAR YEAR AS THE BASIC TIME SCALE, AND ARGUED
22 THAT A MUCH MORE IMPORTANT TIME SCALE TO CONTROL FOR WAS
23 AGE, AND THAT BY TAKING CALENDAR YEAR AS THE TIME SCALE,
24 YOU WERE ESSENTIALLY ADJUSTING OUT A VARIABLE THAT WAS SO
25 HIGHLY CORRELATED WITH CUMULATIVE EXPOSURE THAT YOU WOULD
0173

01 HAVE GREAT DIFFICULTY IN EFFICIENTLY ESTIMATING AN EFFECT
02 OF CUMULATIVE EXPOSURE.

03 BASICALLY, TIME SINCE 1959 IN THE ORIGINAL
04 BLOCK PATTERN OF EXPOSURE ANALYSIS IS BASICALLY CUMULATIVE
05 EXPOSURE. SO CALENDAR YEAR AND CUMULATIVE EXPOSURE
06 VIRTUALLY ALIASK (PHONETIC), EXCEPT FOR THOSE PEOPLE WHOSE
07 EXPOSURE CEASED DURING THE FOLLOW-UP PERIOD.

08 SO ALL OF YOUR INFORMATION WAS COMING BETWEEN
09 RETIREES AND CONTINUING EMPLOYEES, AND I ARGUED FOR
10 ANALYSIS THAT CONTROLLED INSTEAD FOR AGE AS THE PRIMARY
11 VARIABLE, IF YOU WERE GOING TO USE THE COX REGRESSION
12 APPROACH WHICH REQUIRED A PRIMARY EXPOSURE VARIABLE OR
13 USING POISSON REGRESSION TECHNIQUES WHERE YOU COULD MORE
14 FLEXIBLY MODEL THE BASELINE RISKS AS A FUNCTION OF NOT
15 ONLY AGE, BUT CALENDAR YEAR, BIRTH COHORT, AND OTHER
16 FACTORS.

17 AND MUCH OF THAT HAS BEEN DONE IN THE
18 APPENDICES WHICH ARE PROVIDED NOW. AND AS I READ THESE
19 APPENDICES, IT NOW APPEARS THAT DESPITE CONSIDERABLE
20 DEBATE OVER WHAT IS THE MOST PARSIMONIOUS AND MOST
21 UNBIASED WAY TO ESTIMATE THE BASE LINE RATES WE'RE
22 PRESENTED WITH MANY DIFFERENT MODELS WITH ALTERNATIVE
23 AKAIKIAN INFORMATION CRITERIAS TO CHOOSE BETWEEN THEM, THE
24 ACTUAL EFFECT ON THE SLOPE ESTIMATES ARE VERY SMALL.

25 SO I NO LONGER THINK THE CONTROL OF AGE
0174

01 CALENDAR YEARS EFFECTS IS THE BIG QUESTION, BUT WHAT
02 REALLY MATTERS IS THE QUESTION OF BACKGROUND EXPOSURES.

03 AND AT LEAST THAT'S THE POSITION THAT'S TAKEN
04 IN THE STATE REPORT, BUT I FIND IT SOMEWHAT -- A LITTLE
05 BIT CONFUSING HOW TO -- HOW DIFFERENT TREATMENTS OF THE
06 BACKGROUND EXPOSURE QUESTION COULD LEAD TO A DRAMATIC
07 REVERSAL OF THE SIGNIFICANT POSITIVE TO A SIGNIFICANT
08 NEGATIVE EFFECT.

09 AND I'VE INCLUDED A BIT OF MATHEMATICS IN THE
10 THIRD OR FOURTH PAGE OF MY NOTES HERE WHICH TRY TO SHOW
11 HOW THAT COULD COME ABOUT. I WON'T GO THROUGH THESE
12 FORMULA EXPLICITLY NOW, BUT THE BOTTOM LINE IS THAT IF WE
13 ARE VIEWING BACKGROUND EXPOSURES AS A POTENTIAL
14 CONFOUNDER, THEN THE RELEVANT BACKGROUND EXPOSURES IS
15 BACKGROUND EXPOSURE ACCUMULATED SINCE BIRTH, NOT SINCE
16 FIRST EMPLOYMENT.

17 AND IF ONE THEREFORE FAILS TO TAKE INTO
18 ACCOUNT BACKGROUND EXPOSURES PRIOR TO FIRST EMPLOYMENT,

19 YOU ARE IN A POTENTIALLY CONFOUNDING SITUATION, WHERE AGE
20 AT FIRST EMPLOYMENT BECOMES A CONFOUNDER, AND IF NOT
21 ADEQUATELY DEALT WITH BY CONTROL ELSEWHERE IN THE MODEL,
22 THEN ONE CAN GET DRAMATICALLY DIFFERENT RESULTS, DEPENDING
23 ON WHETHER YOU DO OR DO NOT ADJUST FOR BACKGROUND
24 EXPOSURES IN THE INTERIM SINCE FIRST EMPLOYMENT.
25 AND I'M NOT SURE THAT THAT WILL GET TO THE
0175
01 BOTTOM OF WHY SOME ANALYSES LEAD TO THE SIGNIFICANT
02 NEGATIVE AND SOME TO THE SIGNIFICANT POSITIVE RESULTS, BUT
03 I SUSPECT THAT'S PART OF IT.
04 THE OTHER PART OF IT AS WE'VE SEEN A NUMBER
05 OF PICTURES, BOTH SOME IN THE REPORT, SOME THAT
06 KENNY CRUMP HAS OFFERED IN SOME OF HIS SUBMISSIONS, AS
07 WELL AS THE INFAMOUS BLUE SLIDE FROM THIS MORNING, WHICH
08 SUGGESTS THAT WHAT IS REALLY DRIVING THE POSITIVE
09 RELATIONSHIP IS PRIMARILY THE COMPARISON BETWEEN THE TRAIN
10 RIDERS AND THE NON-EXPOSED PART OF THE COHORT, RATHER THAN
11 THE ACTUAL DURATION OF EMPLOYMENT PER SE.
12 I HAVE NOT FORMED AN OPINION ON THIS MYSELF,
13 BUT IT DOES SEEM TO ME THAT IF ONE WERE TO TRY TO RESTRICT
14 AN ANALYSIS ONLY TO THE TRAIN RIDERS, AND LOOK AT DURATION
15 AS THE PRIMARY EXPOSURE VARIABLE, THEN WE'RE BACK IN THE
16 SITUATION OF FUNDAMENTAL MULTICOLLINEARITY, THAT DURATION
17 ESSENTIALLY EQUALS A COMBINATION OF ATTAINED AGE, AGE AT
18 FIRST EMPLOYMENT, CALENDAR YEAR, AND BIRTH COHORT, WHICH
19 ONE CANNOT HOPE TO UNSCRAMBLE FROM THESE ANALYSES.
20 SO THEREFORE, I'M NOT THAT DISTURBED BY THE FAILURE
21 TO FIND A DOSE-RESPONSE RELATIONSHIP AMONGST THE TRAIN
22 RIDERS BECAUSE THE DATA AS STRUCTURED HAVE VERY LITTLE
23 POWER TO DETECT SUCH A DOSE-RESPONSE RELATIONSHIP; THUS
24 I'M NOT HOPELESSLY DISTURBED BY THE FACT THAT MOST OF OUR
25 INFORMATION IS COMING FROM THE EXPOSED VERSUS THE
0176
01 UNEXPOSED COHORT. THAT'S IT. I THINK WE SHOULD HAVE SOME
02 CONCERN OF THE APPROPRIATENESS OF TRYING TO SUMMARIZE THIS
03 COMPLEX DATA SET BY A SINGLE SLOPE ESTIMATE, AND WE HAD A
04 LONG DISCUSSION BEFORE LUNCH ON THAT.
05 NOW, THE OTHER POINTS I THINK I CAN DISPENSE
06 WITH BECAUSE THEY ARE ALL IN MY WRITTEN COMMENTS. I TAKE
07 ISSUE IN THE WRITTEN COMMENTS, FOR THOSE WHO DON'T BENEFIT
08 OF THEM IN FRONT OF YOU, WITH SOME OF THE WAYS THE
09 MULTI-STAGE MODEL HAS BEEN FITTED, AND I THINK HAVING A
10 PREVIEW OF WHAT SOME OF THE OTHER SPEAKERS ARE GOING TO
11 SAY, THEY ARE GOING TO ADDRESS THOSE SAME CONCERNS. I'LL
12 SKIP OVER THAT.
13 I DO THINK THAT MULTI-STAGE MODEL WITH THE
14 LAST STAGE ACTIVE IS NOT A BIOLOGICALLY PLAUSIBLE ONE, AND
15 THE STATE COULD HAVE DONE A BETTER JOB IN TERMS OF FITTING
16 THE MULTI-STAGE MODEL.
17 AND I ALSO HAVE SOME TECHNICAL PROBLEMS WITH
18 THE WAY THE LIFETIME RISK ESTIMATE WAS DERIVED, AND STAN
19 AND I HAVE MADE SOME HEADWAY IN TRYING TO UNDERSTAND OUR
20 DISCREPANCIES SINCE THEN, SINCE I WROTE THESE COMMENTS.
21 BUT THE FINAL CONCLUSION, WHICH IS THAT WHAT
22 IS BEING PASSED OFF AS A LIFETIME RISK ESTIMATE, IS IN
23 FACT, REALLY JUST LIFETIME RISK ACCUMULATED TO AGE 70

24 ONLY. WE SHOULDN'T CALL IT A LIFETIME RISK BECAUSE THE
25 MAJORITY OF LUNG CANCER DEATHS OCCUR AFTER AGE 70, AND AN
0177
01 EVEN LARGER PROPORTION OF THE EXCESS DEATHS WILL OCCUR
02 AFTER AGE 70 BECAUSE THAT'S WHEN RELATIVE RISK IS GOING TO
03 BE HIGHER UNDER A CUMULATIVE DOSE HYPOTHESIS.
04 MY OWN -- MY OWN LITTLE LIFE TABLE
05 CALCULATIONS INDICATE THIS WOULD -- IF YOU REALLY WANTED
06 TO COMPUTE SOMETHING THAT YOU WANTED TO CALL A LIFETIME
07 RISK ESTIMATE, IT WOULD BE ABOUT TWO-AND-A-HALF TIMES
08 HIGHER THAN THE NUMBER YOU GOT BY TRUNCATING THE LIFETABLE
09 AT AGE 70.
10 SO WITH THAT I THINK I'LL STOP. I THINK THIS
11 DOCUMENT HAS COME A LONG WAYS FROM WHERE I'VE SEEN IT
12 BEFORE. THE EVIDENCE FOR CAUSALITY I THINK IS MUCH
13 STRONGER THAN IT WAS BEFORE. THE QUANTITATIVE RISK
14 ASSESSMENT, DESPITE ITS FAULTS, ARE MUCH APPROVED.
15 I THINK WE NEED IN GENERAL TO FIGURE OUT HOW
16 TO DO THESE RISK ASSESSMENTS BECAUSE THESE QUESTIONS,
17 THESE METHODOLOGICAL QUESTIONS GO FAR BEYOND DIESEL, AND
18 THE WORLD IS LOOKING AT HOW THIS ASSESSMENT WILL BE DONE
19 AS A GUIDELINE AS TO HOW WE DO OTHER RISK ASSESSMENTS. SO
20 IT BEHOOVES US TO GET IT RIGHT.
21 DR. FROINES: BILL LOCKETT. IS -- WHAT'S THE
22 STATUS ON KENNY CRUMP?
23 MR. LOCKETT: HE'S LISTENING IN.
24 DR. CRUMP: I'M HERE.
25 DR. FROINES: ARE WE ABLE TO PUT HIM ON A SCREEN OR
0178
01 IS IT GOING TO BE A CONFERENCE CALL?
02 MR. LOCKETT: IT'S AUDIO ONLY.
03 DR. FROINES: AUDIO ONLY.
04 KENNY, CAN YOU HEAR ME?
05 DR. CRUMP: I CAN HEAR YOU FINE. CAN YOU HEAR ME?
06 DR. FROINES: YES. SO WHAT WE'RE DOING IS WE'RE
07 HAVING THE THREE AFTERNOON SPEAKERS SPEAK, AND THEN WE'RE
08 GOING TO HAVE A DISCUSSION FOLLOWING THE THREE TALKS.
09 SO IF YOU'RE WILLING, WILL YOU GO AHEAD NOW?
10 DR. CRUMP: OKAY. I'LL GO AHEAD, AND I'LL GO AS
11 FAR AS I CAN. I'M NOT SURE HOW LONG THAT I CAN STAY ON
12 THE LINE.
13 GREETINGS TO EVERYONE FROM DISNEY WORLD. I'M
14 HERE WITH MY FIVE GRANDKIDS, AND AFTER A COUPLE OF DAYS
15 HERE WITH THEM, I'VE BEEN SORT OF LOOKING FORWARD TO THIS
16 CONFERENCE CALL SO I CAN PROP MY FEET UP FOR A FEW
17 MINUTES. SO THANK YOU VERY MUCH FOR GIVING ME THIS
18 OPPORTUNITY.
19 I'M ALSO HAPPY TO DO THIS BECAUSE I
20 UNDERSTAND THAT PART OF THE IDEA OF THIS MEETING WAS
21 TRYING TO RESOLVE THE SO-CALLED CRUMP/DAWSON DEBATE, AND I
22 THINK REALLY TO RESOLVE ANY DEBATE, YOU NEED TO HEAR BOTH
23 SIDES OF THE STORY. SO I'M HAPPY TO BE HERE AND TELL MY
24 SIDE.
25 MOST -- SOME OF YOU MAY KNOW THIS, BUT JUST
0179
01 FOR SOME OF YOU THAT DON'T, MY BACKGROUND OF MY
02 PARTICIPATING IN THIS ISSUE, ABOUT SIX YEARS AGO I WAS

03 INVITED BY E.P.A. TO USE THE GARSHICK COHORT STUDY TO
04 CONDUCT A RISK ASSESSMENT AND ESSENTIALLY DO WHAT
05 CALIFORNIA HAS BEEN DOING WITH THAT DATA, AND AFTER
06 ANALYZING IT, I DECIDED THAT IT WASN'T APPROPRIATE BECAUSE
07 THERE WAS REALLY NO CONVINCING EFFECT OF DIESEL IN THIS
08 STUDY.

09 AND ON THE BASIS OF THAT, E.P.A. DECIDED NOT
10 TO USE THIS STUDY IN THEIR RISK ASSESSMENT.

11 SINCE THEN THE STATE OF CALIFORNIA HAS BEEN
12 DOING NUMEROUS ANALYSES WHICH WILL BE THE SUBJECT OF THIS
13 MEETING, AND STAN DAWSON AND I HAVE HAD A NUMBER OF
14 DISCUSSIONS AND TRADED ANALYSES ABOUT THE -- ABOUT THE
15 MEANING OF THESE DATA AND IN THE ANALYSES.

16 LET ME FIRST GIVE YOU JUST MY BASIC
17 CONCLUSIONS, BASED ON ALL THE ANALYSIS THAT I'VE DONE, AND
18 ALSO READING ABOUT CALIFORNIA'S ANALYSES.

19 FIRST OF ALL, THE RISK OF -- LUNG CANCER RISK
20 IS SIGNIFICANTLY ELEVATED IN TRAIN RIDERS IN THIS COHORT
21 RELATIVE TO CLERKS AND SIGNALMEN. THE LATTER TWO GROUPS
22 ARE THE ONES USED ARE THE CONTROL GROUP IN THE RECENT
23 GARSHICK ET AL. ANALYSIS.

24 HOWEVER, WITHIN THE GROUP OF EXPOSED TRAIN
25 RIDERS, THERE IS NO DOSE-RESPONSE. THE RISK IN TRAIN

0180
01 RIDERS DECREASES WITH INCREASING EXPOSURE, AND GENERALLY
02 WITHIN INCREASING DURATION OF EXPOSURE. AND THE RISK IN
03 THE HIGHEST OR LONGEST EXPOSED TRAIN RIDERS IS NO
04 DIFFERENT FROM THAT OF THE CLERKS AND SIGNALMEN. RISK WAS
05 NOT SIGNIFICANTLY ELEVATED IN THE SHOP WORKERS, DESPITE
06 THE FACT THAT THESE WORKERS HAD THE MOST INTENSE EXPOSURES
07 FOR SURE, AND I THINK LIKELY THE HIGHEST EXPOSURES OF
08 ALL.

09 THEREFORE, I CONCLUDE THAT THERE IS NO
10 COMPELLING EVIDENCE FOR THE FACT THE DIESEL EXHAUST OF
11 LUNG CANCER IN THIS COHORT.

12 IN ADDITION, THERE WAS AN OBVIOUS PROBLEM
13 WITH THE FOLLOW UP IN THE LAST FOUR YEARS OF THIS STUDY.

14 NOW, I KNOW THAT DR. GARSHICK, I BELIEVE, HAS
15 BEEN DOING SOME WORK TO CORRECT THAT PROBLEM, AND HE MAY
16 HAVE ADDRESSED THAT TODAY. SORRY I WASN'T HERE TO HEAR
17 WHAT HE HAD TO SAY.

18 BUT THE WAY THINGS STAND WITH THE DATA THAT I
19 HAVE, WE DON'T KNOW I DON'T THINK WHAT CAUSED THE PROBLEM,
20 AND WE REALLY DON'T KNOW IF THE PROBLEM IS LIMITED TO THE
21 LAST FOUR YEARS OF THE STUDY.

22 SO I THINK THAT WE SHOULD TRY TO CORRECT THE
23 FOLLOW-UP PROBLEM THE FULL WORK OF THIS STUDY REALLY CAN
24 BE RELIED UPON, AND I HAVE MORE TO SAY ABOUT THAT IN JUST
25 A FEW MINUTES.

0181
01 BACK TO MY COMMENT ABOUT THE SHOP WORKERS.
02 THESE WORKERS WORKED MANY TIMES IN ENCLOSED AREAS WITH
03 RUNNING ENGINES, AND IN THE EARLY DAYS, WORKED IN GARAGES
04 THAT WERE DESIGNED FOR STEAM ENGINES AND DID NOT HAVE
05 ADEQUATE VENTILATION, AND BY ALL ACCOUNTS THEY SUFFERED
06 SOME MUCH HIGHER EXPOSURES THAN THE OTHER -- OTHER
07 WORKERS. THESE WORKERS ALSO HAD POTENTIAL EXPOSURE TO

08 ASBESTOS.

09 NOW, THE -- AS FAR AS I CAN TELL, THE DEBATE
10 OVER THE EXPOSURE OF THE SHOP WORKERS STEMS FROM A SINGLE
11 STATEMENT IN THE ORIGINAL GARSHICK PAPER THAT SAID THAT
12 SOME OF THE WORKERS, SHOP WORKERS, WORKED IN TYPES OF
13 RAILROAD SHOPS THAT HAD NO DIESEL EXPOSURE AS FAR AS
14 ASBESTOS USE. IT JUST SAYS SOME. IT DOESN'T SAY THE
15 SOURCE OF THE INFORMATION OR ANY ESTIMATE OF WHAT
16 PERCENTAGE.

17 BUT THE EXPOSURE DATA THAT WE HAVE THAT WAS
18 COLLECTED IN 1983 ESTIMATED EXPOSURES IN THE SHOP WORKERS
19 RELATIVE TO THE TRAIN RIDERS WAS ABOUT TWICE AS HIGH, AND
20 WE WOULD EXPECT THAT THAT RATIO WOULD BE CONSIDERABLY
21 LARGER IN EARLIER YEARS.

22 SO UNLESS THE SHOP WORKERS -- UNLESS THE
23 MAJORITY OF THE SHOP WORKERS WORKED IN AREAS THAT DID NOT
24 INVOLVE DIESEL EXPOSURE, WE SHOULD EXPECT THEIR EXPOSURES
25 TO BE EQUAL TO OR GREATER THAN, AS A GROUP, THAT OF THE
0182 TRAIN RIDERS.

01 SO CONSEQUENTLY, I THINK THE FACT THAT THE
02 SHOP WORKERS DID NOT HAVE ELEVATED RISKS RELATIVE TO THE
03 CLERKS AND SIGNALMEN ARGUES AGAINST AN EFFECT OF DIESEL IN
04 THIS -- IN THIS COHORT.

05 NOW, I'D LIKE TO TURN TO SOME BIOSTATISTICAL
06 ISSUES, AND I AGREE WITH DR. THOMAS THAT SOME OF THIS IS
07 PRETTY TOUGH GOING, BUT IF YOU TRY TO HANG WITH ME AND --
08 AS I MAKE MY POINTS WITH THIS BECAUSE I THINK IT'S
09 IMPORTANT BECAUSE IN THIS ANALYSIS, I THINK IT'S VERY MUCH
10 THAT THE DEVIL IS IN -- IT'S IN THE DETAILS.

11 I WOULD REFER YOU -- IF YOU HAVE -- IF YOU
12 HAVE THE REPORT, THE REVISED REPORT, I THINK IT WILL HELP
13 IF YOU WILL TURN TO PAGE F-18. THAT'S THE NEXT TO THE
14 LAST PAGE IN THE REPORT, AND YOU'LL SEE TWO DOSE-RESPONSES
15 THERE. I'M GOING TO BE REFERRING TO THOSE A FAIR AMOUNT
16 IN MY DISCUSSION.

17 AT THE TOP OF THE PAGE YOU HAVE THE ORIGINAL
18 ANALYSIS CONDUCTED BY GARSHICK ET AL. IN THE ORIGINAL
19 PAPER.

20 AND THIS ANALYSIS HAS YEARS OF EXPOSURE ON
21 THE X-AXIS AND RELATIVE RISK ON THE Y-AXIS, AND YOU SEE AN
22 INCREASING TREND. THIS WAS A POYSON REGRESSION THAT
23 CONTROLLED FOR -- FOR AGE IN 1959.

24 NOW, IF I'M NOT MISTAKEN, I BELIEVE THIS IS
25
0183 ACTUALLY MY ANALYSIS. IT LOOKS VERY, VERY MUCH LIKE IT,
01 AND ACTUALLY, THIS IS MY REPRODUCTION OF GARSHICK'S
02 ANALYSIS, AND I WAS ABLE TO REPRODUCE IT ALMOST EXACTLY.

03 IF YOU LOOK AT THE FIGURE ON THE BOTTOM, AND
04 I BELIEVE THIS IS MISLABELED, AND I THINK IT WAS ALSO
05 MISLABELED IN MY ORIGINAL SUBMISSION.

06 THIS IS THE SAME IDENTICAL ANALYSIS AS IN THE
07 TOP FIGURE WITH ONE CHANGE. THAT'S A VERY SUBTLE CHANGE.
08 INSTEAD OF CONTROLLING FOR AGE IN 1959, THIS ANALYSIS
09 CONTROLLED FOR ATTAINED AGE. IT HAD THE SAME NUMBER OF
10 VARIABLES ESTIMATED, BUT IT HAD WHAT I THINK IS A
11 SIGNIFICANTLY BETTER -- WELL, A BETTER FIT TO THE DATA.
12

13 THIS WILL MEAN SOMETHING TO STATISTICIANS. THE DEVIANTS
14 IN THE BOTTOM GRAPH IS SMALLER BY 18 THAN THE DEVIANTS IN
15 THE UPPER GRAPH.

16 SO THE METHOD USED IN THE BOTTOM GRAPH GIVE A
17 BETTER DESCRIPTION OF THE UNDERLYING DATA THAN THE ONE IN
18 THE TOP GRAPH. SO I SEE NO REASON TO ACCEPT THE ANALYSIS
19 IN THE TOP GRAPH OVER THAT IN THE BOTTOM GRAPH.

20 NOW, WHAT THE BOTTOM GRAPH SHOWS IS RATHER
21 DRAMATICALLY DIFFERENT. IT SHOWS THE DECREASING TREND
22 WITHIN EXPOSED WORKERS. AND BY THE WAY, THIS PARTICULAR
23 ANALYSIS, BOTH OF THEM WERE LIMITED -- OMITTED SHOP
24 WORKERS FROM THE ANALYSIS, AND I WILL SAY PARENTHETICALLY
25 THAT MOST OF THE ANALYSES THAT I'M GOING TO BE DISCUSSING

0184

01 ALSO ELIMINATED THE SHOP WORKERS. SO WHETHER THE SHOP
02 WORKERS ARE PRESENT IS REALLY NOT AN ISSUE.

03 SO I REALLY THINK THAT IF -- IF THE ORIGINAL
04 ANALYSIS HAD CONTROLLED BETTER FOR -- FOR AGE THEY
05 MIGHT -- THEN WOULD THEY WOULD HAVE GOTTEN -- THEY WOULD
06 HAVE NOT GOTTEN THE POSITIVE DOSE-RESPONSE THAT IS SEEN
07 IN THE PAPER.

08 THIS PARTICULAR RESULT SEEMS TO BE QUITE
09 ROBUST WITH RESPECT TO HOW THE ANALYSIS IS CONDUCTED. THE
10 ONE THAT'S SHOWN HERE IS A COX REGRESSION. IF YOU USE A
11 POISSON REGRESSION USING INTERNAL CONTROLS, YOU GET
12 ESSENTIALLY THE SAME DOSE-RESPONSE. IF YOU USE A POISSON
13 REGRESSION USING EXTERNAL CONTROLS, YOU GET ESSENTIALLY
14 THE SAME RESULT.

15 IN THIS LATTER ANALYSIS IS A VERY DIFFERENT
16 ANALYSIS FROM USING INTERNAL CONTROLS. IT ONLY USES ABOUT
17 THREE -- I THINK THREE VARIABLES AS OPPOSED TO 15 TO 20
18 THAT YOU WOULD USE WITH INTERNAL CONTROLS SO IT'S A VERY
19 DIFFERENT KIND OF ANALYSIS.

20 AND EVEN A VERY SIMPLE ANALYSIS WHERE YOU
21 DON'T DO ANY MODELING AT ALL, AND JUST TAKE THE OBSERVED
22 DEATH AND AGE AND CALENDAR YEAR CATEGORY AND PARTITION
23 THEM INTO THE VARIOUS EXPOSURES EXPECTED -- CALCULATED
24 EXPECTEDS BY DOING THE PARTITIONING JUST BASED UPON THE
25 NUMBER OF PERSON YEARS -- YOU -- I'LL STILL GET A NEGATIVE

0185

01 DOSE-RESPONSE.

02 I THINK WHAT THIS SHOWS IS SOME FAIRLY MINOR
03 CHANGES IN THE WAY AN ANALYSIS DONE WITH THIS COHORT
04 PRODUCES SOME VERY DRAMATIC RESULTS.

05 IT'S VERY IMPORTANT HOW YOU CONTROL FOR AGE
06 AND CALENDAR YEAR. IF YOU LOOK JUST AT TRAIN RIDERS, YOU
07 GET DECREASING TRENDS. IF YOU ELIMINATE THE LAST FOUR
08 YEARS OF FOLLOW UP, THE DECREASING TREND AMONG TRAIN
09 RIDERS IS STATISTICALLY -- STATISTICALLY SIGNIFICANT.

10 NOW, IN THE CALIFORNIA ANALYSIS, THEY GET
11 MANY POSITIVE TRENDS. WHY IS THAT THE CASE WHEN I'M
12 PRESENTING A TREND THAT APPEARED NEGATIVE? I THINK THERE
13 ARE BASICALLY TWO REASONS FOR THAT. AND ALL OF THE
14 ANALYSES THAT ARE PRESENTED IN THE DOCUMENT, YOU'RE
15 BASICALLY COMPARING TRAIN RIDERS TO CLERKS AND SIGNALMEN.

16 BUT IT IS NOTED EARLIER TRAIN RIDERS DO HAVE
17 A HIGHER OVERALL RISK LUNG CANCER RISK, THAN CLERKS AND

18 SIGNALMEN. THAT'S PRETTY EVIDENT FROM LOOKING AT THE
19 FIGURE ON F-3 ON PAGE F-18. AND WHENEVER THAT'S THE
20 CASE -- AND LET'S JUST SUPPOSE FOR THE SAKE OF ARGUMENT
21 THAT THERE REALLY IS -- IS REALLY NO EFFECT OF DIESEL AT
22 ALL, BUT THE ELEVATED RISK AMONG THE TRAIN RIDERS IS DUE
23 TO SOMETHING TOTALLY -- TOTALLY UNRELATED TO DIESEL.
24 IF THAT IS THE CASE, YOU SHOULD EXPECT AT
25 LEAST A FLAT RELATIVE RISK IN HIGHER EXPOSURE CATEGORIES.

0186
01 MAYBE IT SHOULDN'T DECREASE LIKE THIS, BUT IT SHOULD BE AT
02 LEAST FLAT.
03 BUT IF YOU FIT A LINEAR MODEL TO THESE DATA,
04 YOU WILL GET A STATISTICALLY SIGNIFICANT POSITIVE TREND,
05 EVEN THOUGH THERE REALLY IS NO DOSE-RESPONSE WITHIN THE
06 EXPOSED GROUP.
07 AND AS A MATTER OF FACT, IF YOU FIT A LINEAR
08 MODEL TO THE DATA SHOWN IN FIGURE F-83 AT THE BOTTOM OF
09 PAGE F-18 YOU WILL ALSO GET --- PARDON ME? I'M SORRY?
10 DR. GLANTZ: THAT WAS STAN GLANTZ BLOWING HIS
11 NOSE. IT WAS NOT MEANT AS A POLITICAL COMMENT.
12 DR. CRUMP: OKAY. WELL, IT'S PROBABLY TIME WE
13 BREAK ANYWAY.
14 IF YOU FIT A LINEAR MODEL TO THE DATA AS
15 SHOWN IN FIGURE F-3, IT SHOWS THAT DECREASING SLOPE WITHIN
16 THE TRAIN RIDERS, YOU WILL IN FACT GET A SIGNIFICANT
17 POSITIVE TREND.
18 OF COURSE, YOU WILL GET EXCEEDINGLY POOR FIT,
19 BUT YOU WILL GET A POSITIVE TREND.
20 THE OTHER REASON FOR THE DIFFERENCE IS A LACK
21 OF CONTROL FOR A CONTROL COMPOUNDING VARIABLES, AND AS YOU
22 CAN SEE BY COMPARING FIGURES F-2 AND F-3, THAT'S A VERY
23 CRITICAL ISSUE BECAUSE A VERY SEEMINGLY, A VERY MINOR
24 CHANGE IN THE WAY THE ANALYSIS WAS DONE PRODUCE VERY
25 DRAMATICALLY DIFFERENT RESULTS.

0187
01 I'D LIKE TO MENTION NOW THE EXPOSURE METRIC
02 AND THE SUBTRACTING OFF OF BUSINESS AND SUBTRACTING OFF OF
03 THE BACKGROUND. THE WAY THE CALIFORNIA DOCUMENT HAS DONE
04 THAT IS TO SUBTRACT THE -- LET'S ASSUME THAT THE EXPOSURES
05 IN THE CLERK AND SIGNALMEN WAS BACKGROUND AND TO SUBTRACT
06 THAT AMOUNT ALL FROM THE EXPOSURES IN THE -- FROM THE
07 TRAIN RIDERS.
08 BASICALLY, I DON'T HAVE A REAL -- REAL
09 PROBLEM WITH THAT. AT LEAST NOT A -- NOT A BIG PROBLEM.
10 I THINK IT WILL TEND TO -- I THINK IT WILL UNDERESTIMATE
11 THE EXPOSURES -- DIESEL EXPOSURES IN THE -- IN THE CLERKS
12 AND SIGNALMEN BUT -- BECAUSE I THINK THEY WERE EXPOSED.
13 AND I THINK THERE WERE SOME -- I THINK SOME REAL
14 IMPLAUSIBLE DIFFERENCES AMONG THE EXPOSURES AMONG THE
15 DIFFERENT GROUPS OF TRAIN RIDERS. THERE WERE ABOUT SIX
16 DIFFERENT GROUPS OF TRAIN RIDERS, AND THEY WERE DIFFERENT
17 EXPOSURES ESTIMATED FOR THOSE. AND I WOULD HAVE RATHER
18 HAVE SEEN THAT INFORMATION BE TAKEN INTO ACCOUNT INSTEAD
19 OF ASSUMING THEY WERE ALL EXPOSED AT THE SAME LEVEL.
20 DR. FROINES: KENNY?
21 DR. CRUMP: YES.
22 DR. FROINES: CAN YOU FINISH UP IN ABOUT FIVE

23 MINUTES?
24 DR. CRUMP: IT MAY TAKE ME ABOUT TEN. I'LL DO MY
25 BEST.

0188
01 DR. FROINES: WELL, WE'VE TRIED TO HOLD EVERYBODY
02 HERE TO 20 MINUTES -- 15 TO 20 MINUTES FOR THEIR TALKS,
03 AND IT'S NOT REALLY FAIR TO THE OTHER PARTICIPANTS TO HAVE
04 SOMEBODY BASICALLY GO ON AT LENGTH.
05 SO I WOULD LIKE YOU TO FINISH IN FIVE MINUTES
06 IF YOU CAN.
07 DR. CRUMP: I'LL DO MY BEST, BUT IF YOU NEED, JUST
08 CUT ME OFF. YOU JUST DO THAT. I HAVE A COUPLE MORE
09 POINTS THAT I THINK ARE IMPORTANT TO MAKE.
10 OKAY. THE POINT THAT I WAS MAKING WAS THAT I
11 DON'T HAVE A REAL PROBLEM WITH THE WAY THAT'S DONE, AND
12 PERHAPS WITH THE -- I'M NOT SURE THAT THE CHANGES THAT I
13 WOULD MAKE OF THAT WOULD MAKE A LARGE DIFFERENCE.
14 BUT I WANT TO MAKE IT CLEAR THAT THAT IS NOT
15 THE REASON FOR THE NEGATIVE SLOPES THAT I'M GETTING. FOR
16 EXAMPLE, IF YOU TAKE THE CUMULATIVE EXPOSURES AND APPLY
17 THOSE JUST TO THE -- THE ANALYSES THAT I DID EARLIER AND
18 APPLY THOSE JUST TO THE -- TO THE TRAIN RIDERS, YOU GET
19 ALL NEGATIVE SLOPES. MANY OF THEM ARE SIGNIFICANT AND
20 THEY ARE HIGHLY SIGNIFICANT.
21 AND THESE ANALYSES, UNLIKE WHAT DUNCAN WAS
22 SAYING WITH THE USING YEARS OF EXPOSURE, YOU DO NOT HAVE
23 THE SAME KIND OF THE CO-VARYING -- CO-VARIANCE BETWEEN
24 CALENDAR YEAR AND CUMULATIVE EXPOSURE, AND I COULD GO INTO
25 THAT IN MORE DETAIL, BUT WHEN YOU DO THAT, YOU GET ALL

0189
01 NEGATIVE SLOPES.
02 AND LET ME ALSO SAY, FOR EVERYTHING THAT I'VE
03 DONE INDICATES THAT WITHIN THE GROUP OF EXPOSED WORKERS,
04 YOU GET A NEGATIVE TREND WITH INCREASING DURATION OF
05 EXPOSURE OR INCREASING YEARS OF EXPOSURE, NOT INDICATIVE
06 OF THE EFFECT OF EXPOSURE TO DIESEL IN LUNG CANCERS, IT
07 SEEMS TO ME.
08 BUT LET ME ALSO POINT OUT THAT THESE NEGATIVE
09 TRENDS ARE NOT LIMITED TO LUNG CANCER. I'VE LOOKED AT A
10 NUMBER OF OTHER END POINTS, AND YOU GET NEGATIVE TRENDS
11 WITH MANY OTHER VERY SIMILAR NEGATIVES TRENDS, WITH MANY
12 OTHER KINDS OF INFLUENCES, THE DEGESTIC LUNG CANCER, THE
13 SKIN AND HEART DISEASE, STROKE, ALL CAUSES OF DEATH, ALL
14 OF THESE GIVE ESSENTIALLY THE SAME KINDS OF NEGATIVE
15 TRENDS WITHIN THE TRAIN RIDERS.
16 DR. BLANC: THEY SHOULD BE LIVING FOREVER THEN,
17 SHOULDN'T THEY, BECAUSE THE LONGER YOU WORK, THE SAFER YOU
18 WOULD BE. THIS IS DR. BLANC QUESTIONING. DOESN'T THAT
19 MAKE YOU SUSPICIOUS THAT, IN FACT, THERE IS SOMETHING
20 SYSTEMATICALLY WRONG WITH YOUR ANALYSIS, AND COULD YOU
21 PROVIDE US WITH THE R-SQUARE VALUE FOR THE CORRELATION
22 BETWEEN THE PREDICTIVE VARIABLE THAT YOU'RE ADJUSTING FOR
23 IN TERMS OF CALENDAR YEAR AND IN TERMS OF CUMULATIVE
24 EXPOSURE?
25 DR. CRUMP: YEAH. I WOULD BE HAPPY TO PROVIDE

0190
01 THAT. THIS PARTICULAR KIND OF ANALYSIS DOESN'T PRODUCE AN

02 R-SQUARE.
03 DR. BLANC: NO, BUT YOU COULD GIVE ME THAT USING
04 THE TWO VARIABLES JUST A CORRELATION, JUST SO I CAN GET A
05 SENSE OF THE COLLINEARITY.
06 DR. CRUMP: YEAH, I WOULD BE VERY PLEASED TO DO
07 THAT.
08 DR. BLANC: PERHAPS YOU COULD SUBMIT THAT
09 SEPARATELY.
10 DR. CRUMP: OKAY. WHAT TWO VARIABLES WERE YOU
11 REFERRING TO?
12 DR. BLANC: WELL, ACTUALLY, WHY DON'T YOU JUST GIVE
13 US AN INTERCORRELATION MATRIX FOR ALL OF THE PREDICTIVE
14 VARIABLES IN YOUR MODEL?
15 DR. CRUMP: OKAY. THAT CAN BE DONE.
16 I THINK WHAT IS -- I THINK IT'S VERY
17 TROUBLING TO ME WHAT IT SUGGESTS TO ME THAT THERE IS
18 SOMETHING WRONG WITH THE DATA. AND WE KNOW THERE'S
19 SOMETHING WRONG WITH THE FOLLOW UP IN THE LAST FOUR
20 YEARS. I DON'T KNOW WHAT DR. GARSHICK HAS UNCOVERED IN
21 HIS WORK SO FAR OR HE HAS TALKED ABOUT IT HERE.
22 BUT I'VE BECOME CONCERNED THAT THERE IS
23 SOMETHING BASICALLY WRONG WITH THE DATA IN THIS -- IN THIS
24 STUDY.
25 I HAVE JUST A COUPLE OF OTHER -- MORE QUICK
0191 COMMENTS. WHAT DUNCAN SAID ABOUT THE -- ABOUT THE
01 MULTI-STAGE MODEL, THE COMMENTS I HAD PREVIOUSLY MADE TO
02 CAL E.P.A., AND I CERTAINLY AGREE WITH THOSE.
03 I THINK THAT THE ANALYSIS THAT THEY NOW HAVE
04 IN THERE ARE BETTER, BUT IT'S -- IN FACT, THEY STILL HAVE
05 NOT -- I DON'T THINK CONTROLLED ADEQUATELY FOR COMPOUNDING
06 VARIABLES. AND I THINK THE ANALYSIS THAT I DID LAST
07 SUMMER IS BASICALLY THE ANALYSIS THAT DUNCAN HAS SAID HE
08 WISHED THEY WOULD HAVE DONE. AND I GET MUCH LESS EVIDENCE
09 OF AN EFFECT OF DIESEL THAN WHAT IS SEEN IN THE ANALYSES I
10 THINK IN THIS REPORT.
11 FINALLY -- THIS IS MY FINAL POINT. I JUST
12 WANT TO COMMENT ON THE ANALYSIS THAT'S PRESENTED IN PAGES
13 7-25, WHICH IS CALLED A CURRENT APPROACH.
14 THE ANALYSIS THAT'S PRESENTED THERE APPEARS
15 TO BE THE SORT OF -- THE MAIN ANALYSIS SINCE IT IS IN THE
16 BODY OF THE REPORT, AND THE OTHER ANALYSES ARE RELEGATED
17 TO THE APPENDIX.
18 I MAY HAVE MISSED SOMETHING, BUT I CANNOT
19 UNDERSTAND WHAT WAS DONE. I DON'T THINK IT'S EXPLAINED
20 CAREFULLY ENOUGH, AND AS I MENTIONED, THE DEVIL IS THE
21 DETAIL IN THESE ANALYSES, AND I THINK YOU'VE JUST GOT TO
22 LAY IT OUT SO THEY CAN BE -- CAN BE UNDERSTOOD.
23 THERE ARE A COUPLE OF POINTS THAT I JUST --
24 IN GENERAL I DON'T UNDERSTAND IT, BUT THERE -- I DON'T
0192 UNDERSTAND WHAT WAS DONE. IT SAYS THAT THERE IS -- THIS
01 WAS A PROXIMATE ANALYSIS. I DON'T KNOW IN WHAT SENSE IT
02 WAS PROXIMATE.
03 IT SAYS AT ONE POINT THAT THE ONE YEAR OF --
04 ANY EXPOSURE IN A YEAR WAS COUNTED AS A FULL YEAR OF
05 EXPOSURE. SINCE YOU KNOW WHAT THE EXPOSE -- HOW LONG, HOW

07 MANY MONTHS IN A YEAR A PERSON WAS EXPOSED, I DON'T
08 UNDERSTAND WHY IT WAS NECESSARY TO -- TO DO THAT.
09 AND THEN IN THE RESULTS ON THE -- THE TABLE
10 THAT GIVES THE RESULTS, IT SAYS, FOR EXAMPLE, THAT -- THIS
11 IS ON PAGE 7-49 OF TABLE 7-10, I'M TALKING ABOUT THE --
12 THE ANALYSES GIVEN UNDER LABEL TWO THERE.
13 IT SAYS EITHER -- IT SAYS IT'S ATTAINED AGE
14 AND CALENDAR YEAR, OR AGE AT START OF STUDY IN CALENDAR
15 YEAR. I DON'T UNDERSTAND HOW IT COULD BE BOTH OF THOSE,
16 AND I FOUND THAT VERY PUZZLING.
17 SO, I WOULD LIKE TO GET SOME MORE DETAILS ON
18 THAT ANALYSIS BEFORE I COULD REALLY COMMENT ON IT.
19 AND IF YOU WOULD LIKE TO HAVE WRITTEN
20 COMMENTS, I'D BE GLAD TO PROVIDE THOSE. I WOULD LIKE TO
21 HAVE MORE DETAILS ON THAT ANALYSIS, AND I THINK IT WOULD
22 BE HELPFUL GIVEN THE TIME THAT I HAVE, I HAVE A LITTLE BIT
23 MORE TIME TO PROVIDE WRITTEN COMMENTS. I'M GOING TO BE
24 OUT AGAIN NEXT WEEK FOR SEVERAL DAYS ALSO.
25 DR. FUCALORO: MAY I ASK A QUESTION? THIS IS
0193
01 ANTHONY FUCALORO ON THE S.R.P.
02 YOU AT THE BEGINNING OF YOUR TALK GAVE US TWO
03 CONCLUSIONS, AND MAYBE I HAVE THEM WRONG, BUT LET ME READ
04 THEM TO YOU AND SEE IF I DO HAVE THEM -- AND SEE IF I IN
05 FACT HAVE THEM RIGHT.
06 TRAIN RIDERS HAVE ENHANCED RISK FOR LUNG
07 CANCER OVER CLERKS, BUT THERE IS NO DOSE-RESPONSE THAT YOU
08 CAN DETECT; AND SECOND, THAT NO ENHANCED RISK FOR SHOP
09 WORKERS ARGUES AGAINST -- AND MAYBE I HAVE THIS WRONG --
10 DIESEL EXHAUST BEING A CARCINOGEN.
11 DO I HAVE THOSE CONCLUSIONS CORRECT, OR I DID
12 I MISWRITE THEM?
13 DR. CRUMP: WELL, IT'S PRETTY CLOSE. I DIDN'T SAY
14 DIESEL EXHAUST BEING A CARCINOGEN, BUT I SAID AN EFFECT OF
15 DIESEL IN THIS STUDY.
16 DR. FUCALORO: OKAY. NOW -- THEN LATER ON IN YOUR
17 TALK, AND I KNOW YOU DIDN'T HAVE TIME TO FINISH IT -- YOU
18 TALKED ABOUT THIS NEGATIVE RESPONSE, WHICH OBVIOUSLY SAID
19 SOMETHING IS WRONG SOMEWHERE. NOW, WHETHER IT'S WRONG
20 WITH THE ANALYSIS OR WITH THE DATA, I'LL ASSUME FOR THE
21 MOMENT -- WITH ALL DUE APOLOGIES TO DR. GARSHICK -- THAT
22 THERE IS SOMETHING WRONG WITH THE DATA, THEN HOW CAN ONE
23 DRAW THE -- DOES THAT NOT VITIATE YOUR CONCLUSIONS THAT
24 YOU STATED AT THE BEGINNING, IF THERE'S SOMETHING WRONG
25 WITH THE DATA?
0194
01 DR. CRUMP: WELL, IF THERE IS SOMETHING WRONG WITH
02 THE DATA, I DON'T THINK WE CAN MAKE ANY CONCLUSIONS AT ALL
03 PROBABLY. IT WOULDN'T BE WISE TO MAKE ANY CONCLUSIONS AT
04 ALL FROM THE ANALYSIS, FROM THE DATA.
05 DR. FUCALORO: BUT DIDN'T YOU SAY THERE WAS
06 SOMETHING WRONG WITH THE DATA, OR DID I MISUNDERSTOOD YOU?
07 DR. CRUMP: I AM CONCERNED THAT THERE WAS SOMETHING
08 WRONG WITH THE DATA, AND THE -- THAT'S THE ONLY WAY I CAN
09 EXPLAIN THE RESULTS THAT I'M GETTING. THERE MUST BE
10 SOMETHING WRONG WITH THE DATA.
11 DR. FROINES: I'M CONCERNED THAT WE'RE NOW IN A

12 QUESTION PERIOD BEFORE DALE'S GIVEN HIS TALK.
13 KENNY, ARE YOU GOING TO STAY ON THE PHONE?
14 DR. CRUMP: YEAH. I CAN STAY ON FOR A WHILE.
15 DR. FROINES: IF THERE'S ONLY GOING TO BE ONE
16 QUESTION FROM STAN, THEN WE'LL DO IT. BUT OTHERWISE, I
17 DON'T WANT TO OPEN -- I DON'T WANT TO START OPENING THIS
18 UP.
19 STAN, YOU WANT TO -- IS THIS QUICK?
20 DR. GLANTZ: YEAH. I ACTUALLY HAVE TWO, BUT I'LL
21 ONLY ASK ONE.
22 DR. FROINES: WELL, I THINK IT'S IMPORTANT TO
23 ASK --
24 DR. GLANTZ: I'LL ASK ONE.
25 DR. FROINES: I THINK IT'S IMPORTANT TO ASK ALL THE
0195
01 QUESTIONS. IT'S JUST THAT I DON'T WANT TO HAVE DALE
02 PENALIZED --
03 DR. GLANTZ: ALL RIGHT.
04 DR. FROINES: -- GIVEN -- BECAUSE OF THE LOGISTICS
05 OF THIS SITUATION.
06 DR. GLANTZ: WELL -- WELL, YOU'VE LOOKED -- IF YOU
07 LOOK AT FIGURE F-4, WHICH IS THE COMBINATION OF F-2 AND
08 F-3, EXCEPT PUT ON THE SAME SCALE, YOU'LL NOTICE THAT
09 REALLY THE DIFFERENCES THAT YOU'VE BASED YOUR ARGUMENT ON
10 DON'T LOOK QUITE SO IMPRESSIVE BECAUSE THE -- IF YOU LOOK
11 AT THE CONFIDENCE INTERVALS FROM THE POINT ESTIMATES,
12 THEY -- THEY REALLY OVERLAP QUITE A LOT EXCEPT MAYBE AT
13 THE VERY LAST POINT WHERE THEY STILL OVERLAP, BUT A LITTLE
14 BIT LESS. AND WE'VE ALREADY HEARD THAT THE LONG-TERM
15 FOLLOW-UP DATA, WERE A LITTLE BIT SUSPECT ANYWAY.
16 AND IF YOU LOOK AT F-4, DON'T YOU THINK IT
17 WOULD BE REASONABLE TO CONCLUDE THAT AT LEAST OUT TO A
18 12-YEAR EXPOSURE, THE TWO MODELS REALLY YIELD QUITE
19 SIMILAR RESULTS?
20 DR. CRUMP: WELL, I'M NOT SURE EXACTLY WHERE F-4
21 COMES FROM BECAUSE IT'S OBVIOUSLY NOT THE SAME AS F-3 AND
22 F-2. SO I WAS -- I WAS ALSO PUZZLED BY THAT.
23 DR. GLANTZ: NO. IT'S THE SAME AS F-3 AND F-2.
24 IT'S JUST THE SCALES -- F-3 AND F-2 HAVE DIFFERENT SCALES.
25 DR. CRUMP: WELL, WHY IS THE RELATIVE RISK IN F-3
0196
01 1.5 AT THE LOWEST EXPOSURE, LOOKS LIKE IT'S 1.3 IN -- IN
02 F-4?
03 DR. GLANTZ: WELL, NO. IT'S RELATIVE -- WELL, I
04 MEAN, MAYBE IT'S THE RELATIVE RISK MINUS ONE.
05 DR. CRUMP: RIGHT. RIGHT. AND IT'S .3 WHERE IS
06 IT'S .5 IT APPEARS TO ME LOOKING AT TABLE --
07 DR. GLANTZ: YOU KNOW, YOU'RE RIGHT. I THINK THE
08 STAFF MADE A MISTAKE WHEN THEY MADE THIS GRAPH. IT WASN'T
09 MEANT TO BE THE SAME. OH, I THOUGHT THEY WERE.
10 WELL, I THEN -- WHY DON'T WE GO ON AND LET ME
11 CLARIFY THIS BECAUSE I MISUNDERSTOOD THE GRAPH.
12 DR. CRUMP: OKAY.
13 DR. FROINES: THEN, KENNY, YOU'RE OFF FOR THE
14 MOMENT, BUT IF YOU CAN HANG ON, WE'LL GET BACK WITH YOU
15 WITH ANY OTHER QUESTIONS.
16 DR. CRUMP: I'LL SEE IF I CAN HANG ON. IF

17 SOMETHING COMES UP, I'LL APOLOGIZE IN ADVANCE FOR BREAKING
18 OFF, AND I'LL TRY TO HANG ON.

19 DR. FROINES: DALE HATTIS FROM CLARK UNIVERSITY IS
20 OUR NEXT AND LAST SPEAKER.

21 DR. HATTIS: YEAH. I WANTED BASICALLY TO TRY TO DO
22 THREE THINGS. I SHOULD -- I HAVE TO PUT ON THE
23 MICROPHONE.

24 ALL RIGHT. AH, YES, THAT WILL BE MUCH
25 BETTER. I NEED TO WALK AROUND. I MIGHT SAY, IT'S
0197 PREFACED THAT I'M ONE OF THOSE DREADFUL PEOPLE WHO MASSAGE
01 DATA. SOME PEOPLE EVEN SAY DREDGE DATA, AND SOME PEOPLE
02 WOULD EVEN SAY TORTURE DATA TO TRY TO GET SOME KIND OF A
03 REASONABLE PICTURE OF THE WORLD IN OUR UNCERTAINTIES
04 BECAUSE I THINK AS TECHNICAL PEOPLE, WE HAVE A OBLIGATION
05 TO SHARE WITH WHY OUR COMMUNITY -- WHAT WE THINK WE HAVE
06 ESTABLISHED WITH GREAT CONFIDENCE, BUT ALSO TO SAY WITH
07 APPROPRIATE CAVEATS WHERE WE THINK THE LIKELIHOODS ARE AND
08 WHAT THE DISTRIBUTION OF THE POSSIBLE STATES OF THE WORLD,
09 MERELY IS.

11 AND I'M GOING TO TRY TO DO THREE THINGS.
12 FIRST I'M GOING TO COMMENT ON SOME OF THE ISSUES IN
13 CONTROVERSY THAT YOU'VE ALREADY HEARD DISCUSSED TODAY.

14 SECOND, I'M GOING TO PRESENT A LITTLE
15 ANALYSIS OF MINE, WHERE I TRY TO INTERPRET
16 CAL-E.P.A.'S ANALYSIS IN TERMS OF AN OVERALL PROBABILITY
17 DISTRIBUTION OF LIKELY POTENCIES, GIVEN ESSENTIALLY SOME
18 REPRESENTATION OF -- OF WHAT I CAN READ INTO THEIR
19 DOCUMENT IN TERMS OF THE RELATIVE WAITINGS OF DIFFERENT
20 POSSIBILITIES; FOR EXAMPLE, FOR THE KIND OF MODEL THAT WAS
21 USED, THE KIND OF ANALYSIS, THE HEIGHT OF THE ROOF, AND I
22 THINK THAT THAT CAN PROVIDE A LITTLE BIT MORE CONSOLIDATED
23 AND ACCESSIBLE PIECE OF INFORMATION. NOT FOR THIS STAGE
24 OF ANALYSIS, BUT -- OF YOUR DECISION MAKING, BUT PERHAPS
25 FOR THE NEXT STAGE WHERE YOU'RE -- WHERE PEOPLE ARE
0198 WANTING TO SHARPEN THE PENCIL AND DO SOME RISK MANAGEMENT.

02

03 AND FINALLY, I'LL INDICATE HOW AN ANALYSIS
04 BASED UPON MY OWN JUDGMENTS OF THE LIKELIHOODS MIGHT TEND
05 TO DIFFER SOMEWHAT WHAT FROM CAL-E.P.A.'S ANALYSIS.

06 FIRST FOR THE ISSUES IN CONTROVERSY, FIRST I
07 WANT TO SAY A LITTLE BIT ABOUT THE, QUOTE, "THRESHOLD
08 QUESTIONS," ABOUT DO YOU HAVE ENOUGH DATA DO TO A RISK
09 ANALYSIS IN SOME SENSE. AND THIS IS SUBDIVIDED INTO THREE
10 PARTS AND I -- PART OF THE ADVANTAGE OF HAVING SOME GRAY
11 HAIRS IS THAT I REMEMBERED THE EARLY '80'S IN WHICH A
12 WHOLE ISSUE OF RISK ANALYSIS IS DEVOTED TO QUANTITATIVE
13 RISK ASSESSMENTS FOR DIESEL EXHAUST.

14 AND THEY WERE BASED AT THE TIME ON THE
15 COMPARATIVE POTENCY METHOD WHERE ONE USES THE MUTAGENIC
16 POTENCY OF DIESEL EXHAUST PARTICLES IN RELATION TO THE
17 POTENCIES OF CIGARETTE SMOKE AND COAL PARTIGE (PHONETIC)
18 FOLLICLES, AND THEY DID -- THEY USED THE EXISTING -- THE
19 THEN EXISTING NEGATIVE EPIDEMIOLOGY, AND LO AND BEHOLD,
20 THEY CAME UP NOT VERY DIFFERENTLY IN TERMS OF THE RANGE OF
21 POTENCIES TO WHAT IS BEFORE US TODAY.

22 SO I THINK THAT, YOU KNOW, THEY HAD ENOUGH
23 INFORMATION TO DO SOME KIND OF A REASONABLE QUANTITATIVE
24 ANALYSIS AT THAT TIME WITH SOME STATEMENT OF
25 UNCERTAINTIES, AND I THINK WE CAN DO A LITTLE BIT BETTER
0199
01 TODAY, BUT I THINK WE DON'T COME UP WITH A HUGE
02 DIFFERENT SET OF ANSWERS TODAY.
03 YOU ALWAYS WANT TO HAVE BETTER INFORMATION,
04 AND I THINK THAT WE CAN PRODUCE BETTER INFORMATION, BUT I
05 THINK THAT TENDS TO AT LEAST GIVE SOME INFORMATION ABOUT
06 THE STABILITY AND THERE IS NO MAGIC POTION, MAGIC QUANTUM
07 OF INFORMATION THAT ONE ABSOLUTELY HAS BEFORE ONE WRITES
08 DOWN A NUMBER, OR BETTER YET, A SET OF NUMBERS THAT FAIRLY
09 ENCOMPASSES ONE'S UNCERTAINTY.
10 SO HOW MUCH -- I WILL BE QUICK ABOUT THIS.
11 HOW MUCH RESIDUAL QUANTITATIVE -- QUALITATIVE UNCERTAINTY
12 SHOULD WE HAVE ABOUT WHETHER DIESEL EXHAUST HAS SOME
13 AMOUNT OF CARCINOGENIC ACTIVITY IN HUMANS? AND I THINK WE
14 HAVE A REASONABLE STATEMENT FROM STAN GLANTZ'S QUESTION
15 ABOUT CONSENSUS THAT, YOU KNOW, AS A BETTING PERSON, YOU
16 BET THAT THERE IS SOME CARCINOGENIC ACTIVITY IN DIESEL
17 EXHAUST.
18 HOW MUCH UNCERTAINTY SHOULD WE HAVE THAT
19 THERE IS A TRUE CANCER POTENCY? BY THAT, WE MEAN A LINEAR
20 INCREMENTAL CONTRIBUTION TO CARCINOGENIC -- TO LUNG CANCER
21 FROM THESE PARTICLES, REGARDLESS OF WHAT THAT POTENCY IS.
22 AND I THINK AGAIN, WE HAVE TO HAVE RELATIVELY
23 LITTLE UNCERTAINTY ON THAT POINT, PARTLY BECAUSE WE HAVE
24 THE FUNDAMENTAL MECHANISMS OF MUTAGENESIS THAT ARE
25 INVOLVED, AND WE HAVE GOOD UNDERSTANDING OF HOW THOSE WORK
0200
01 QUANTITATIVELY IN THE SENSE THAT WE KNOW AT THE HEART OF
02 THE PROCESS, IF THERE IS IN FACT A REACTION OF A -- D.N.A.
03 REACTIVE SUBSET WITH D.N.A., THAT IS A LINEAR PROCESS.
04 THERE IS ALL KINDS OF NONLINEARITIES THAT CAN
05 INTERVENE AT HIGH DOSES BETWEEN THE EXPOSURE AND THE
06 ULTIMATE DEVELOPMENT OF TUMORS, BUT TO MAKE A LONG STORY
07 SHORT, YOU CAN SHOW THAT EACH OF THOSE HAS TO GO LINEAR AT
08 THE LIMIT OF LOW DOSES, BASICALLY, BECAUSE AT THE LIMIT OF
09 LOW DOSES, YOU CAN'T GET SATURATION OF EITHER TOXIFYING OR
10 INTOXIFYING A PROCESS, AND THERE'S ALWAYS GOING TO BE SOME
11 INTERACTION OF REDUCED MUTAGENIC HITS WITH THE BACKGROUND
12 PROCESSES THAT LEAD TO LUNG CANCERS IN THE BACKGROUND
13 PROCESS.
14 SO I THINK THAT THE -- THAT THE ISSUE OF
15 WHETHER THERE'S A THRESHOLD IS REALLY A NONISSUE, AND WE
16 REALLY OUGHT TO BELIEVE THAT THERE IS SOME LINEAR SLOPE.
17 AND FINALLY, HOW HAVE THESE PARTICULATES
18 CHANGED OVER THE YEARS, IS THERE SOME REASON FOR CONCERN
19 THAT THEY'VE CHANGED QUALITATIVELY ENOUGH TO MAKE IT
20 REALLY A DIFFERENT SUBSTANCE, SO THAT OUR PAST INFORMATION
21 IS NOT RELEVANT TO THE CURRENT.
22 AND I THINK AGAIN, WE HAVE SOME EVIDENCE THAT
23 THE DIESEL PARTICULATES MAY WELL HAVE CHANGED TOWARD LOWER
24 PARTICLE SIZES. IF ANYTHING, THAT MAY TEND TO DELIVER
25 THEM TO -- WITH SOMEWHAT GREATER EFFICIENCY TO LOWER DOWN
0201

01 IN THE LUNG -- I THINK WE HAVE NO EVIDENCE THAT THAT GIVES
02 YOU A QUALITATIVELY DIFFERENT SITUATION. IF ANYTHING, IT
03 SUGGESTS THAT YOU MIGHT WANT TO ADJUST THE POTENCIES
04 SLIGHTLY UPWARD TO ACCOUNT FOR THE GREATER DEPOSITION
05 EFFICIENCY AND THE LIKELY GREATER PERSISTENCE OF THE
06 SMALLER DISTRIBUTION PARTICLES IN THE LUNG.

07 ALL RIGHT. I HAVE 15 MINUTES. ALL RIGHT.
08 SO I WANT I WANT TO COMMENT ON DAWSON VERSUS CRUMP, AND I
09 WON'T GO OVER THE POINTS THAT DR. DUNCAN HAS SO CAPABLY
10 COVERED, BUT I DO HAVE SOME INSIGHT INTO THIS IN MUCH MORE
11 SIMPLE-MINDED TERMS OF THIS ISSUE OF BACKGROUND
12 SUBTRACTION.

13 AND THAT'S BASICALLY IN THIS SECOND SLIDE. A
14 TALE OF TWO CLERKS AND AN ENGINEER. LET'S IMAGINE THAT WE
15 HAVE CLERK A, AGE 60 IN 1990 -- 1980. HE HAD FIVE YEARS
16 SELLING TICKETS IN THE STATION, AND 35 YEARS IN A CITY
17 DEPARTMENT STORE UNDER THE ANALYSIS THAT DR. CRUMP HAS
18 USED. AS I UNDERSTAND IT, THAT WOULD BE COUNTED AS 165
19 MICROGRAM YEARS PER CUBIC METER OF EXPOSURE. DAWSON WOULD
20 CALCULATE ZERO. OKAY.

21 UNDER CLERK B, AGE 60 IN 1980, 20 YEARS
22 SELLING TICKETS WOULD BE COUNTED AS HAVING AN EXPOSURE
23 THAT IS MUCH MORE THAN THAT, AND IT'S ALMOST COMPARABLE TO
24 TEN YEARS AS AN ENGINEER, WHEREAS DAWSON AGAIN WOULD COUNT
25 HIM AS HAVING NO DIESEL EXPOSURE.

0202

01 I THINK THAT THE JUDGMENT OF THE WORKING
02 GROUP THAT DID THE STUDY WAS THAT THE CLERKS WERE NOT
03 SUBSTANTIALLY EXPOSED. AND IN THAT CASE, I THINK IT IS
04 PROBABLY A BIT OF AN ERRORS IN VARIABLES PROBLEM IF YOU IN
05 FACT TREAT THEM AS DR. CRUMP HAS TREATED THEM IN THE
06 OVERALL ANALYSIS.

07 AND I THINK THAT THERE'S SOME OTHER DATA THAT
08 SUPPORTS THE IDEA THAT, IN FACT, THEY PROBABLY WEREN'T
09 EXPOSED TO VERY MUCH. THEY MIGHT HAVE BEEN EXPOSED A BIT,
10 BUT NOT TO VERY MUCH, AND THAT IS THESE DATA THAT --

11 DR. GLANTZ: WHAT ABOUT ENGINEER C? YOU DIDN'T
12 FINISH THE SLIDE.

13 DR. HATTIS: YEAH. ENGINEER C HAS ESSENTIALLY --

14 DR. GLANTZ: I MEAN, IF YOU DIDN'T WANT TO TELL
15 US --

16 DR. HATTIS: I JUST WANTED TO SAY THAT -- THE
17 COMPARISON I WANTED TO MAKE WITH THAT IS -- THAT IN THE
18 THIRD ONE, ENGINEER C HAS AN EXPOSURE THAT'S ONLY -- WITH
19 10 YEARS OF DIESEL EXPOSURE IS ONLY A LITTLE MORE THAN THE
20 SECOND CLERK IN THE DAWSON ANALYSIS WHEREAS IT COMES OUT
21 WITH A POSITIVE AMOUNT OF -- OF -- IT'S ONLY A LITTLE MORE
22 THAN A CLERK IN THE CRUMP ANALYSIS; WHEREAS IT COMES OUT
23 WITH A CONSIDERABLE AMOUNT OF EXPOSURE IN THE DAWSON
24 VARIANT OF THE ANALYSIS.

25 SO I THINK -- I WANTED TO ADDUCE SOME DATA,

0203

01 IN ADDITION TO THE JUDGMENT OF THE RESEARCH GROUP THAT THE
02 CLERKS WERE NOT MATERIALLY EXPOSED. I WANTED TO INTRODUCE
03 A LITTLE BIT OF DATA, AND THIS WAS THE SAME DATA THAT WAS
04 REFERRED TO BY KATHIE HAMMOND. THIS IS A SERIES OF
05 MEASUREMENTS OF RESPIRABLE PARTICULATES IN RURAL SMALL

06 TOWNS IN TENNESSEE. THESE ARE NOT PRISTINE SMALL TOWNS.
07 THEY HAVE BIG MINES AND THINGS LIKE THAT NEARBY.
08 AND WHAT I DO WANT TO SAY IS THAT YOU NOTICE
09 THAT THE MEAN RESPIRABLE PARTICULATES MEASURED OUTDOORS --
10 THIS IS THE SAME KIND OF DEVICE THAT KATHIE HAMMOND AND
11 COMPANY USED -- IT'S ABOUT 17 OR 18 MICRO GRAM PER CUBIC
12 METER.
13 AND SO THAT IS VERY COMPATIBLE WITH WHAT SHE
14 PRESENTED US, SOMETHING BETWEEN 10 AND 20 AS THE LIKELY
15 OUTDOOR BACKGROUND THAT PROBABLY SHOULD BE -- LEVELS THAT
16 SHOULD BE SUBTRACTED FROM THE VALUE OF THE TRAIN RIDERS.
17 OKAY.
18 AT THE SAME TIME, THE NONSMOKE -- THERE IS
19 DATA FOR THOSE PEOPLE WOULD ARE FROM PERSONAL AND INDOOR
20 MEASUREMENTS FROM PEOPLE WHO WERE BOTH SMOKE EXPOSED AND
21 PEOPLE WHO WERE NOT SMOKE EXPOSED; AND WHAT YOU WILL
22 NOTICE IS THE MEAN FOR THE PERSONAL INDOOR MEASUREMENTS
23 WITH A NONSMOKE EXPOSED PEOPLE WAS ABOUT IN THE -- IN THIS
24 RANGE OF THE LOW 30'S ON AVERAGE.
25 AND THAT IS VERY SIMILAR TO WHAT WAS MEASURED
0204
01 FOR THE CLERKS. SO I THINK THERE'S GOOD REASON TO BELIEVE
02 THAT IF THE CLERKS WERE EXCESSIVELY EXPOSED, THEY WERE NOT
03 EXPOSED TO VERY MUCH. AND I THINK IT'S -- IT'S QUITE
04 REASONABLE UNDER THESE CIRCUMSTANCES TO TREAT THEM AS, IN
05 FACT, UNEXPOSED TO DIESEL-SIZED PARTICLES. THE FOUR
06 MICRON, 50 PERCENT CUTOFF DEVICE WILL ESSENTIALLY BE
07 MEASURING LOTS OF PARTICULATE THAT IS PROBABLY FROM
08 CRUSTAL SOURCES AND PROBABLY HAS VERY DIFFERENT
09 PROPERTIES, BOTH CHEMICALLY AND -- AND IN ITS DEPOSITION
10 FROM THE DIESEL-SIZED PARTICLES.
11 AND SO THAT'S THE BASIC DISCUSSION THERE.
12 WHAT I NOW WANT TO DO IS BRIEFLY PRESENT
13 RESULTS OF A VERY SIMPLE-MINDED PROBABILITY TREE ANALYSIS
14 OF UNCERTAINTIES INVOLVED THAT HAVE BEEN ANALYZED BY THE
15 CAL-E.P.A. GROUP.
16 THIS INVOLVES DIFFERENT CHOICES OF DATA SETS
17 FOR QUANTITATIVE PROJECTIONS, CHOICES AMONG STATISTICALLY
18 AND BIOLOGICALLY PLAUSIBLE MODELS OF DOSE-RESPONSE,
19 CHARACTERIZATION OF EXPOSURE AMOUNTS AND TIME PATTERNS,
20 SOME STATISTICAL UNCERTAINTIES IN THE FIT FOR ANIMAL AND
21 RANDOM ERRORS, AND THERE IS SOME ROOM FOR, OF COURSE,
22 CHARACTERIZING THE POSSIBILITY OF UNSUSPECTED SYSTEMATIC
23 ERROR, THAT I WON'T GO INTO AT THE MOMENT.
24 THIS IS BASICALLY HOW THE TREE LOOKS LIKE,
25 WHICH IS BASICALLY MY READING OF CAL-E.P.A.'S VIEW ON
0205
01 THESE -- ON A FEW OF THESE ISSUES.
02 BASICALLY, THIS IS DIVIDED INTO THE ANALYSES
03 IN CHAPTER 7 VERSUS THE ANALYSES IN CHAPTER D -- APPENDIX
04 D, AND I THINK THAT CAL-E.P.A. NOW EXPRESSES SOME
05 PREFERENCE FOR THE APPENDIX D ANALYSES.
06 I THINK THEY CLEARLY IS -- A MORE IMPORTANT
07 PREFERENCE IS 80 PERCENT 20 PERCENT THAT I'VE ASSIGNED IT
08 FOR THE ARMITAGE-DOLL MODELS VERSUS THE GENERAL EMPIRICAL
09 MODELS, AND THEY HAVE SOME SLIGHT PREFERENCE AT LEAST FOR
10 THE UNUSUAL SEVEN-STAGE AFFECTED MODEL VERSUS THE

11 SIX-STAGE AFFECTED.
12 IN ADDITION TO THAT, THERE'S UNCERTAINTIES,
13 AND THIS IS HOW I'VE REPRESENTED THEM IN THE BASE EXCESS
14 EXPOSURES OF THE TRAIN RIDERS VERSUS THE CLERKS THAT
15 I'VE -- I'VE RATED HERE AS GIVING ABOUT 50 PERCENT WEIGHT
16 TO THEIR MEDIAN ESTIMATE THAT THEY DO MOST OF THE
17 CALCULATIONS ON. I THINK THAT'S PROBABLY THE LOW -- OR
18 HIGH -- LOW, 30 PERCENT WEIGHT TO THE MINIMAL POSSIBILITY;
19 THAT IS, IF YOU DIDN'T -- IF YOU SUBTRACTED THE FULL CLERK
20 LEVEL FROM THE -- FROM THE TRAIN RIDER LEVEL, AND
21 20 PERCENT WEIGHT TO THE OTHER BOUND, ESSENTIALLY, WHERE
22 YOU SUBTRACT NOTHING FROM THE TRAIN RIDER EXPOSURES.
23 AS TO THE HEIGHT OF ROOF, I THINK CAL-E.P.A.
24 CLEARLY PROVIDES -- GIVES A PREFERENCE FOR A HEIGHT OF THE
25 ROOF ABOUT THREE, BUT THEY HAD SOME WEIGHT ON TWO AND
0206
01 FIVE, AND WE'LL ADMIT THAT THE OUTSIDE THE POSSIBILITY OF
02 THE EFFECTIVE HEIGHT OF THE ROOF WOULD BE EITHER ONE OR
03 TEN, AND THAT'S HOW THAT'S REPRESENTED IN THE MODEL.
04 SO BASICALLY ONE DOES A SERIES OF -- AND THEN
05 THERE'S STATISTICAL SAMPLING ERROR BECAUSE THE LOWER
06 CONFIDENCE LIMITS AND THE UPPER CONFIDENCE LIMITS ARE
07 BASICALLY SYMMETRICAL IN NEARLY ALL THE MODELS I
08 REPRESENT, PRELIMINARILY AS NORMAL DISTRIBUTIONS AND --
09 WHICH IS UNUSUAL FOR ME. I USUALLY REPRESENT EVERYTHING
10 AS LOG NORMAL, BUT IN THIS CASE I COULDN'T DO THAT.
11 AND SO THIS IS THE BASIC TENOR OF THE
12 RESULTS. THE UPPER GRAPH ESSENTIALLY IS A INTERPRETED
13 PROBABILITY DENSITY FUNCTION FOR THE UNCERTAINTY IN THIS
14 LOW-DOSE SLOPE AS DONE FROM THESE ALTERNATIVES THAT I'VE
15 JUST OUTLINED WHERE YOU CAN SEE THE CUTOFF THERE IS -- IS
16 AT -- BASICALLY, YOU SEE IT LOOKS LIKE KIND OF A LOG
17 NORMAL, VAGUELY SKEWED SHAPE. IF YOU PLOTTED ON LOG
18 GRAPH, YOU SEE THERE ARE TWO HUMPS IN THE GRAPH THAT
19 CORRESPOND, I BELIEVE, ROUGHLY TO THE CASES FOR THE
20 MULTI-STAGE MODEL VERSUS THE OTHER MODELS THAT WERE USED,
21 ALTHOUGH THERE IS A LOT OF MIXING IN THERE.
22 IN NUMBERS, THIS IS WHAT YOU GET --
23 DR. GLANTZ: I DON'T WANT TO INTERRUPT YOU, BUT I
24 DIDN'T UNDER- -- COULD YOU JUST EXPLAIN WHAT THAT GRAPH IS
25 A LITTLE MORE?
0207
01 DR. HATTIS: OKAY. THIS IS A GRAPH, HOW LIKE --
02 YOU KNOW, GIVEN -- THIS IS A RESULTS OF A MONTE CARLO
03 SIMULATION WHERE ESSENTIALLY 10,000 TIMES YOU'RE TAKING A
04 RANDOM CHOICES AT EACH OF THESE BRANCHES OF THE TREE, AND
05 CALCULATING, AND THEN ALSO CALCULATING FROM A RANDOM
06 CHOICE OF THE STATISTICAL UNCERTAINTY WITHIN THAT
07 PARTICULAR BRANCH, WHAT THE POTENCY WOULD BE.
08 SO THIS IS THE REPRESENTATION OF OUR
09 UNCERTAINTY GIVEN THE CAL-E.P.A. ANALYSIS IN THE CANCER
10 POTENCY FACTOR.
11 DR. GLANTZ: SO WOULD THAT MEAN -- AND I DON'T WANT
12 TO SLOW YOU DOWN, BUT I JUST WANT TO UNDERSTAND THIS.
13 DR. HATTIS: SURE.
14 DR. GLANTZ: WHAT THAT MEANS IS -- WELL, NO. I
15 MEAN, THIS IS AN IMPORTANT POINT. I MEAN, WHAT YOU'RE

16 SAYING IS IF YOU TAKE ALL OF THE DIFFERENT ALTERNATIVES
17 MODELS THAT THEY DESCRIBED IN THE APPENDIX, AND THEN YOU
18 MONTE CARLO -- YOU SAY, LET'S JUST FLIP A COIN TO DECIDE
19 WHICH ASSUMPTIONS TO MAKE --
20 DR. HATTIS: RIGHT. EXACTLY.
21 DR. GLANTZ: -- THAT YOU'RE 90 -- UPPER 95 PERCENT
22 CONFIDENCE ESTIMATE FOR THE CANCER POTENCY IS --
23 DR. HATTIS: IS ABOUT SIX TIMES --
24 DR. GLANTZ: -- ABOUT SIX TIMES TEN TO THE MINUS
25 FOUR --
0208
01 DR. HATTIS: YEAH, IN ROUND NUMBERS.
02 DR. GLANTZ: -- WE'VE GOTTEN ALMOST REGARDLESS --
03 OF WHICH SPECIFIC MODEL ASSUMPTIONS YOU MAKE?
04 DR. HATTIS: RIGHT. RIGHT. AND THE ADVANTAGE OF
05 THIS -- THERE IS TWO ADVANTAGES OF THIS KIND OF TREATMENT.
06 FIRST, I THINK IT PROVIDES A
07 CONSOLIDATED DISTRIBUTION THAT I THINK IS EASY TO
08 UNDERSTAND.
09 AND SECONDLY, IT CAN ALSO BE INTERPRETED IN
10 TERMS OF OTHER PERCENTILES OF THE DISTRIBUTION THAT WE
11 MIGHT CARE ABOUT MORE THAN -- I MEAN, I KNOW THAT
12 CALIFORNIA CARES A LOT ABOUT THE 95TH PERCENTILE, BUT
13 THERE ARE OTHER THINGS ONE COULD CARE ABOUT.
14 FOR EXAMPLE, FOR COST BENEFIT CALCULATIONS,
15 ONE MIGHT WANT TO ARRIVE AT SOME ESTIMATE OF THE MEAN;
16 RIGHT? THE MEAN COMES OUT TO BE SOMETHING LIKE TWO TIMES
17 TEN TO THE MINUS FOUR, OKAY? AND FORGIVE MY EXPRESSING
18 THESE TWO SIGNIFICANT FIGURES, BUT YOU SHOULD UNDERSTAND
19 THAT THESE ARE PROBABLY NOT ACCURATE TO THAT, BUT I DON'T
20 WANT TO -- I DON'T WANT TO LOSE WHATEVER INFORMATION
21 THAT'S THERE.
22 SO BASICALLY, THE MEAN COMES OUT TO BE ABOUT
23 TWO TIMES TEN TO THE MINUS FOUR. IF YOU WANT -- IF YOU
24 WANT A 90 PERCENT CONFIDENCE RANGE, CONTINGENT UPON MY
25 GUESSING CORRECTLY ABOUT WHAT CAL-E.P.A.'S WEIGHT SHOULD BE
0209
01 FOR THE DIFFERENT CHOICES, YOU GET ABOUT 20-FOLD RANGE
02 BETWEEN THREE TIMES TEN TO THE MINUS FIFTH, AND ABOUT SIX
03 TIMES TEN TO THE MINUS FOURTH FOR THE 95TH PERCENTILE TO
04 THE 5TH PERCENTILE RATIO.
05 THAT'S NOT VERY DIFFERENT FROM WHAT WE DID IN
06 19 -- WHAT WAS DONE IN 1983. OKAY. BUT IT'S -- I THINK
07 BASED UPON -- I THINK IT FAIRLY CAPTURES THE
08 UNCERTAINTIES, AT LEAST AS WE'VE ANALYZE THEM.
09 NOW, I THINK THERE'S A FURTHER PIECE OF
10 UNCERTAINTIES THAT WE MIGHT WANT TO INCLUDE --
11 DR. BLANC: COULD YOU JUST CLARIFY THE UNITS AGAIN?
12 THAT WOULD BE --
13 DR. HATTIS: THIS IS IN TERMS OF UNIT RISK.
14 DR. BLANC: SO THAT WOULD BE 2.3 CASES OF LUNG
15 CASES PER 10,000 PER MICROGRAM YEAR OF EXPOSURE, OR IS IT
16 SOME OTHER --
17 DR. HATTIS: YEAH. 2.3 TIMES TEN TO THE MINUS
18 FOURTH RISK OF LUNG CANCER PER MICRO -- PER LIFETIME
19 EXPOSURE --
20 DR. BLANC: OH, PER --

21 DR. HATTIS: -- AS MODIFIED BY YOUR 70-YEAR
22 LIFETIME EXPOSURE, PER MICROGRAM PER CUBIC METER OF
23 EXPOSURE. ASSUMING THAT WE DIRECTLY PROJECT THAT. YOU
24 KNOW, THERE'S A FEW DIFFERENT UNCERTAINTIES THAT ARE NOT
25 FULLY QUANTITATIVELY CAPTURED HERE, AND I'M GOING TO
0210
01 ALLUDE TO THE POSSIBILITIES OF DOING A SOMEWHAT MORE
02 EXPANDED ANALYSIS INCORPORATING SOME ADDITIONAL
03 CONSIDERATIONS.
04 FIRST, OF COURSE, I THINK -- I THINK WE OUGHT
05 TO USE THAT SPENGLER -- THOSE SPENGLER ET AL. DATA TO FORM
06 OUR ESTIMATE OF HOW MUCH BACKGROUND EXPOSURE THE TRAIN
07 RIDERS HAD BECAUSE I THINK THEY WERE EXPOSED PRIMARILY TO
08 OUTDOOR BACKGROUND, NOT INDOOR BACKGROUND LIKE THE CLERKS
09 WERE, BECAUSE I SEE THESE LOCOMOTIVES, AND MY PICTURE OF
10 THE LOCOMOTIVES IS THE ENGINEERS ARE HANGING OUT THE
11 WINDOW, AND HE'S MOSTLY -- NOT A VERY TIGHTLY SEALED
12 COMPARTMENT IN ANY EVENT.
13 SO I THINK THAT MOSTLY WE OUGHT TO COUNT THEM
14 AS BEING EXPOSED TO -- IN ADDITION TO CIGARETTE SMOKE, TO
15 BACKGROUND -- OUTDOOR RURAL BACKGROUND AT THIS TIME.
16 I THINK THAT THE -- WE SHOULD HAVE CONTINUOUS
17 RATHER THAN DISCRETE REPRESENTATIONS OF SOME OF THE
18 PARAMETERS OF NATURALLY CONTINUOUS -- LIKE, OBVIOUSLY, THE
19 HEIGHT OF THE ROOF CAN TAKE ON VALUES OTHER THAN TWO,
20 THREE, FIVE; RIGHTSO? WE SHOULD HAVE SOME CONTINUOUS
21 FUNCTION TO REPRESENT THAT.
22 I THINK THERE SHOULD BE SOME WEIGHTING OF
23 OTHER RELATIVE RESPONSES OF INFORMATION. I THINK THAT THE
24 META-ANALYSIS AMPLIFIED BY KATHIE HAMMOND'S ANALYSIS OF
25 THE LIKELY EXPOSURES FOR DIFFERENT GROUPS DESERVES, YOU
0211
01 KNOW, SOME WEIGHT IN THE OVERALL PICTURE, AND I THINK THAT
02 THERE'S AN OPPORTUNITY TO DO THAT.
03 I THINK -- WITH APOLOGIES TO DR. MAUDERLY, I
04 THINK SOME WEIGHT STILL DESERVES TO BE PUT ON THE ANIMAL
05 DATA. I'M NOT PREPARED TO SAY THAT'S WORTH ENOUGH TO --
06 TO BE -- TO MAKE A BIG DEAL ABOUT IT, BUT I THINK IT'S --
07 I THINK THAT THERE IS STILL A BIT OF, YOU KNOW, SOME -- I
08 THINK THAT THE WAY ONE DOES THAT CREATIVELY, I THINK, IT'S
09 BY LOOKING AT THE COMPARISONS OF OTHER CARCINOGENS, FOR
10 EXAMPLE, THAT HAVE BEEN MEASURED IN RATS AND FOR WHICH WE
11 HAVE HUMAN MEASUREMENTS; FOR EXAMPLE, RADON AND CIGARETTE
12 SMOKE, AND SAY, OKAY, HOW DOES THE COMPARATIVE POTENCY
13 WORK? YOU KNOW. HOW DOES THAT PROJECTION WORK BASED ON
14 THOSE OTHER BETTER STUDIED THINGS -- I STILL THINK THAT
15 THERE'S A CONCERN THAT THERE'S SOME NONLINEARITIES GOING
16 ON IN THE DATA, BUT YOU KNOW.
17 ANYHOW, I'M NOT -- I DON'T THINK IT'S -- I
18 THINK IT'S VERY -- I THINK IT'S -- I THINK IT'S NOT TOO
19 NECESSARY TO TAKE THE VIEW THAT THE RAT DATA ARE
20 COMPLETELY WORTHLESS.
21 FINALLY, I THINK THAT THE -- THERE IS -- SOME
22 WEIGHT SHOULD BE PUT ON THE ORIGINAL COMPARATIVE MUTAGENIC
23 POTENCY STUDIES.
24 AND I THINK FINALLY, WE ALSO OUGHT TO
25 CONSIDER THE POSSIBLE IMPLICATIONS OF THE CHANGES IN THE

0212

01 DISTRIBUTION OF LIKELY RELATIVE POTENCY OF NEW DIESEL
02 PARTICLES, WITH A TENDENCY TOWARDS SMALLER PARTICLE SIZES
03 THAT MIGHT HAVE SOME IMPLICATIONS FOR THE POTENCY OF THE
04 NEW PARTICLES VERSUS THE OLD PARTICLES.

05 SO THOSE ARE MY EXPECTED UNCERTAINTIES THAT I
06 WOULD LIKE TO PURSUE IN SOME FURTHER WORK. I'VE GOT A
07 BUNCH OF OTHER SLIDES THAT YOU CAN SEE THAT ARE LEFT OVER
08 FROM MY PRESENTATION IN 1994.

09 AND IF ANY OF THEM -- AND THEY TEND BASICALLY
10 TO GO TO THE ISSUE OF MAYBE WE SHOULDN'T BE SO CONVINCED
11 THAT IF DIESEL WERE ACTING AS, YOU KNOW -- IN THIS WAY
12 THAT WE SHOULD NECESSARILY FIND A CONTINUING INCREASE IN
13 LUNG CANCERS WITH DOSE AMONG THE TRAIN RIDERS.

14 THERE'S LOTS OF POSSIBLE THINGS THAT CAN
15 DISTORT THE RELATIONSHIP, PARTICULARLY AT HIGH LEVELS IN
16 THE DIRECTION OF SORT OF BENDING IT OVER A BIT. AND THOSE
17 GET TO BE A LITTLE BIT ARCAINE.

18 AND SO I WOULD BE HAPPY TO ANSWER QUESTIONS
19 ABOUT THOSE THINGS, BUT I DON'T TRY TO PRESENT THEM NOW.

20 DR. FROINES: THANK YOU. THERE IS A LOT OF
21 SLOUCHING GOING ON IN THIS ROOM.

22 DR. GLANTZ: COULD I JUST ASK YOU ONE CLARIFYING
23 QUESTION?

24 DR. FROINES: SURE.

25 DR. GLANTZ: WHEN YOU DID YOUR -- YOU KNOW, YOU

0213

01 MAKE THE POINT WHEN YOU DID THE SIMULATION THAT YOU
02 ASSUMED THESE CERTAIN WEIGHTS AND PERCENTAGES.

03 HOW SENSITIVE ARE YOUR RESULTS TO THOSE
04 ASSUMPTIONS?

05 DR. HATTIS: YEAH, I'VE DONE SEPARATE SENSITIVITY
06 ANALYSIS THAT YOU'LL FIND IN THE DOCUMENT, BUT BASICALLY,
07 IT WOULD TAKE EXTREME READINGS OF THE CAL-E.P.A. DOCUMENT
08 THAT ARE ALL IN THE DIRECTION OF MAKING IT TOWARD LOWER
09 ESTIMATES OR ALL IN THE DIRECTION OF MAKING TOWARD HIGHER
10 ESTIMATES. YOU CAN CHANGE THOSE NUMBERS ABOUT
11 TWO-AND-A-HALF FOLD.

12 DR. GLANTZ: BUT IT'S NOT AN ORDER OF MAGNITUDE?

13 DR. HATTIS: WELL, THAT'S -- YEAH. THAT'S WHAT YOU
14 GET. THAT'S WHAT I GOT.

15 DR. GLANTZ: THAT'S IMPORTANT.

16 DR. FROINES: OKAY. WE'RE IN THE PERIOD NOW WHERE
17 I THINK IT'S BASICALLY AN OPEN DISCUSSION BETWEEN THE
18 SPEAKERS AND THE PANELISTS WITH RESPECT TO THE LAST THREE
19 SPEAKERS, KENNY CRUMP, DUNCAN THOMAS, AND -- YEAH, I'LL
20 GET TO THAT -- AND DALE HATTIS. AND WE HAVE DOWN HERE
21 COMMENTS BY STAN DAWSON.

22 BEFORE WE GET ANY QUESTIONS WHERE -- I DON'T
23 KNOW -- IS STAN IN THE ROOM? STAN, DO YOU WANT TO MAKE
24 COMMENTS AT THIS POINT?

25 TAKE PETER KENNEDY'S MICROPHONE. HE IS

0214

01 GONE. OR UNLESS YOU WANT TO COME HERE.

02 DR. DAWSON: OH, YEAH. MAYBE I OUGHT TO.

03 DR. FROINES: I THINK PEOPLE ARE WINDING DOWN. SO
04 MAKE THEM AS POIGNANT AS POSSIBLE.

05 DR. GLANTZ: YOU SAY POIGNANT. SHOULD YOU START TO
06 CRY OR --
07 DR. DAWSON: OKAY. WELL, THERE'S BEEN A LOT OF --
08 WELL, FIRST OF ALL, I WANT TO THANK THE PANEL SPEAKERS. I
09 THOUGHT IT WAS AN OUTSTANDING SERIES OF PRESENTATIONS.
10 AND AS THE PERSON FOLLOWING THAT, I'M VERY -- VERY
11 GRATEFUL.
12 I -- I PROBABLY WILL BE FOCUSING MOST OF MY
13 COMMENTS ON THE ACTUAL QUANTITATIVE RISK ASSESSMENT THAT
14 WAS BROUGHT UP BY DR. CRUMP AND DR. THOMAS.
15 LET ME -- LET ME JUST START WITH I THINK THAT
16 DR. CRUMP KIND OF POINTED OUT SOME OF THE MAJOR ISSUES,
17 AND SO LET ME JUST START WITH THAT.
18 THE -- THE PRIMARY ANALYSES THAT WE'RE
19 TALKING ABOUT --
20 DR. FROINES: STAN, HOLD ON.
21 KENNY, ARE YOU STILL ON THE PHONE?
22 DR. CRUMP: STILL HERE.
23 DR. FROINES: OKAY. THANK YOU.
24 DR. DAWSON: THE PRIMARY ANALYSES THAT I STARTED TO
25 TALK ABOUT -- OR THAT THEY TALKED ABOUT AT FIRST WERE
0215
01 BASED ON A BLOCK -- WHAT I CALLED THE BLOCK PATTERN OF
02 EXPOSURE; THAT IS, AS DR. THOMAS SAID, THE EXPOSURE FROM
03 1959 TO 1960 BEING A DURATION EXPOSURE.
04 AND HE POINTED -- DR. THOMAS POINTED OUT THAT
05 THAT WAS SUSCEPTIBLE TO A LOT OF VAGARIES, AND WE'VE SEEN
06 ONE OF THE VAGARIES IS THAT IF YOU DO IT ONE WAY IT KIND
07 OF LOOKS LIKE IT COMES DOWN, AND IF YOU DO IT ANOTHER WAY
08 IT LOOK LIKE IT GOES UP.
09 BUT IN FACT, THOSE ARE VERY SUBJECTIVE
10 JUDGMENTS, AND IF YOU NEED -- IF YOU DO THE STATISTICAL
11 ANALYSIS, YOU FIND THAT THE SLOPES, THROUGH ALL THIS MASS
12 OF POINTS TURNS OUT TO BE POSITIVE. IT'S SIGNIFICANTLY
13 POSITIVE.
14 SO I -- AND THE MAIN ANALYSIS IN THE REPORT
15 TAKES UP FROM THERE, AND SAYS, WELL, ALL RIGHT. IF THAT'S
16 THE CASE, HOW CAN WE TRY TO STABILIZE THE -- EVEN THAT
17 ANALYSIS AND -- AND THAT'S BEEN -- THAT WAS DONE BY
18 CONTINUOUS -- USING CONTINUOUS VARIABLES OF AGE AND
19 CALENDAR YEAR.
20 AND IT TURNS OUT THAT THE SLOPES THAT YOU GET
21 THERE ARE VERY SIMILAR TO THE ONES THAT YOU GET IN THE
22 APPENDIX D, WHICH HAS THE VERY EXTENSIVE ANALYSES BASED ON
23 ASSUMING SPECIFIC EXPOSURE PATTERNS AND DOING A FULL
24 CALCULATION.
25 SO ANYWAY, THAT'S ONE OF THE BIG POINTS THAT
0216
01 I WANTED TO MAKE WAS THAT THE ANALYSES ARE RATHER -- IF
02 YOU TAKE THAT PRECAUTION WITH THE -- EVEN THE BLOCK
03 ANALYSIS, YOU GET RATHER SIMILAR SORTS OF ANSWERS FOR
04 RISK.
05 NOW, THE -- THE -- ONE OF THE POINTS THAT'S
06 IMPLICIT IN A LOT OF DR. CRUMP'S CRITICISM OF OUR WORK IS
07 THAT THE DOSE-RESPONSE DOESN'T JUST GO SMOOTHLY UP. AND
08 IN FACT, IT HAS A TENDENCY TO HUMP OVER AT THE END. AND
09 DR. HATTIS ALLUDED TO EXPLAINING THE DROP OFF, AND I WOULD

10 JUST LIKE TO SHOW YOU ONE SLIDE THAT WAS DIFFICULT TO PUT
11 IN THE REPORT BECAUSE IT'S ABOUT CIGARETTE SMOKING.
12 NOW, THIS IS A SLIDE OF -- THIS IS A SLIDE OF
13 BASICALLY RISK WHICH IS PLOTTED IN SORT OF A -- A SOMEWHAT
14 STRANGE SCALE OVER HERE CALLED -- CALLED ODDS-RATIO, THIS
15 IS CASE CONTROL STUDY -- VERSUS PACK YEARS OF CIGARETTE
16 SMOKING.
17 NOW, WE ALL KNOW THAT CIGARETTE SMOKING IS
18 PRETTY CARCINOGENIC, AND SO WE'RE PLOTTING -- THIS IS THE
19 LUNG CANCER RATE, AND WE SEE THIS RISE UP TO A PEAK, 12.2,
20 DIFFICULT FOR CIGARETTE KIND OF STUDIES, AND THEN FALLING
21 DOWN TO 1.6.
22 AND THE REASON THAT IS GIVEN IN THE PAPER FOR
23 THIS STUDY IS THAT -- THAT THERE IS A SUSCEPTIBLE
24 POPULATION IN THE GENERAL POPULATION THAT IS RELATIVELY
25 SMALL PART OF THE GENERAL POPULATION WHICH HAS THIS
0217
01 PARTICULAR GENETIC POLYMORPHISM IN IT, AND THAT -- THAT --
02 THOSE ARE THE FOLKS THAT GET THE LUNG CANCER BECAUSE THEY
03 ARE SUSCEPTIBLE, AND THEN THEY DIE OFF.
04 SO THE REST OF THE POPULATION THEN IS GOING
05 HAPPILY ALONG AND NOT GETTING THE CANCER. AND SO THAT'S
06 WHY THIS OVERALL RATE COMES BACK DOWN.
07 SO THAT'S -- THAT'S JUST THE MAIN POINT I
08 WANTED TO MAKE ABOUT THAT SHAPE OF THE CURVE. THAT'S ONE
09 POSSIBLE EXPLANATION WHICH I THINK IS FAIRLY LIKELY, AND
10 THIS IS LUNG CANCER AND SO ON. AND THERE ARE SEVERAL
11 OTHER EXAMPLES THAT ONE CAN USE FOR THIS TO EXPLAIN THAT
12 SORT OF HUMP OVER.
13 AND SO WHAT DO WE DO ABOUT THIS? WELL, WHAT
14 WE DID IN THE REPORT WAS WE SIMPLY DREW A STRAIGHT LINE
15 THROUGH THAT MASS OF POINTS, WHICH WAS CHARACTERIZED BY
16 THE CATEGORICAL STEP FUNCTION AND -- AND THAT WAS OUR BEST
17 WAY OF GETTING THE SLOPE.
18 SO I THINK THAT, IN THE INTEREST OF TIME THAT
19 THAT'S -- THAT'S THE END OF MY COMMENTS.
20 DR. FROINES: THERE WILL PROBABLY BE FEWER TEARS
21 THAT WAY.
22 SERIOUSLY THOUGH. SO LET'S HAVE THE MIKE
23 BASICALLY OPEN FOR DISCUSSION BETWEEN PARTICIPANTS AND
24 PANEL.
25 STAN?
0218
01 DR. GLANTZ: WELL, I -- I HAVE HAD A CHANCE TO
02 CLARIFY THAT -- IS KENNY CRUMP STILL ON THE PHONE?
03 DR. CRUMP: I'M STILL HERE.
04 DR. GLANTZ: OKAY. WELL, I CLARIFIED THAT MY LAST
05 QUESTION ABOUT FIGURE F-4, AND INDEED THE -- THAT WAS
06 RECALCULATED BY O.E.H.H.A.
07 BUT I -- SO LET ME REPHRASE THE QUESTION.
08 IF YOU LOOK AT F-2 AND F-3, WHICH ARE YOUR
09 CALCULATIONS, I BELIEVE, AND JUST REPLOT THOSE TWO FIGURES
10 ON THE SAME GRAPH ON THE SAME SCALE, YOU'LL SEE THAT THE
11 ESTIMATES, IF YOU LOOK AT THE CONFIDENCE BOUNDS THERE,
12 DON'T REALLY DIFFER THAT MUCH EXCEPT MAYBE AT THE VERY
13 HIGHEST DOSE.
14 AND SO I MEAN, DON'T YOU THINK WOULD -- TO ME

15 THAT SUGGESTS THAT THERE REALLY ISN'T THAT MUCH DIFFERENCE
16 BETWEEN THESE TWO APPROACHES, AND THAT YOU'RE BASICALLY
17 JUST LOOKING AT NOISE.

18 I MEAN, WHAT DO YOU -- HOW DO YOU REACT TO
19 THAT STATEMENT?

20 DR. CRUMP: WELL, I THINK FIRST OF ALL, YOU'RE
21 COMPARING AN ANALYSIS -- ONE OF THE ANALYSIS, BITS OF
22 THAT, AT LEAST IN TERMS OF THE DEVIANTS, QUITE A BIT
23 BETTER THAN THE OTHER ANALYSIS.

24 SO I THINK YOU'RE COMPARING IN THAT SENSE A
25 SUPERIOR ANALYSIS TO AN INFERIOR ANALYSIS.
0219

01 AND THE OVERALL QUESTION IS -- WHAT I'M
02 CLAIMING IS IS THAT THERE IS A DECREASING TREND WITHIN THE
03 EXPOSED GROUP, AND THAT TREND IS STATISTICALLY SIGNIFICANT
04 IN MANY ANALYSES.

05 YOU KNOW, WHETHER, YOU KNOW, IT LOOKS
06 COMPARABLE IN A PICTURE LIKE THAT, I REALLY DON'T THINK IS
07 MATERIAL. I THINK IF -- THEY MAY LOOK ABOUT THE SAME. I
08 THINK IF THE ORIGINAL GARSHICK ET AL. PAPER HAD CONDUCTED
09 THE ANALYSIS OF THE DECREASING TREND RATHER THAN AN
10 INCREASING TREND, WHICH I THINK IS THE CERTAINLY THE
11 SUPERIOR ANALYSIS, AND WHAT THE DATA INDICATE, I THINK
12 THEY WOULD HAVE DRAWN MAYBE A DIFFERENT CONCLUSION THAN
13 WHAT THEY DREW.

14 DR. GLANTZ: MAYBE YOU COULD -- WOULD DR. GARSHICK
15 LIKE TO REACT TO THAT?

16 DR. GARSHICK: I THINK THERE WERE TWO ANALYSIS
17 PRESENTED. ONE WAS JUST BASED ON EXPOSURE YES, NO, BASED
18 ON JOB IN 1959, AND THAT SEEMED TO SHOW AN ELEVATED RISK
19 IN THE WORKERS.

20 AND THEN THE YEARS OF EXPOSURE THROUGH '59
21 SHOWED -- IS IT IN FIGURE F-2, AND SINCE THEN, WE'VE COME
22 TO REALIZE THAT THAT 15- TO 17-YEAR EXPOSURE POINT HAS A
23 FIVE-YEAR LAG. SO IT'S REALLY PEOPLE DYING IN 1978 TO
24 '80, THERE'S SUBSTANTIAL UNDERESTIMATION OF NATURAL EVENTS
25 IN THOSE YEARS.

0220
01 AND FURTHERMORE, WE WERE -- WE STARTED
02 COUNTING YEARS OF EXPOSURE IN '59 BECAUSE WE WERE
03 UNCOMFORTABLE EXTRAPOLATING BACK BEFORE 1959, EVEN THOUGH
04 CONSIDERABLE EXPOSURE OCCURRED.

05 SO ONE OF THE FOUR YEARS, YOU COULD ADD
06 ANOTHER TEN YEARS ON TO THAT IN SOME CASES, DEPENDING ON
07 IF THEY COULD HAVE HAD DIESEL EXPOSURE THROUGH 1949 --
08 STARTING IN '49 FOR EXAMPLE.

09 SO THAT WOULD TEND TO CAUSE EXPOSURE
10 MISCLASSIFICATION AND FLATTEN OUT THE CURVE MAKING THE
11 CATEGORIES MORE SIMILAR.

12 AND SO WE TRIED TO GO ONE STEP FURTHER BY
13 CONDUCTING THAT ANALYSIS IN THE BLUE SIDE, AS YOU CALL IT,
14 THAT EXTRAPOLATED EXPOSURE BACK TO THE BEGINNING -- WHEN I
15 PREDICT DIESEL WOULD START FOR WORKERS, AND IT SEEMED TO
16 BE A RATHER FLAT -- FLAT SLOPE.

17 SO I THINK THAT'S THE HISTORY OF THE YEARS
18 OF EXPOSURE ANALYSIS, AND ONE CAN DEBATE THE MERITS OF
19 THAT, BUT I THINK TO TRY TO -- IF YOU'RE INTERESTED IN

20 GETTING SOME SORT OF DOSE-RESPONSE, I THINK WE HAVE TO GET
21 THOSE DEATHS IN THE 15- TO 17-YEAR GROUP, AND EVEN GO
22 BEYOND.
23 DR. GLANTZ: YEAH, BUT ISN'T IT THE -- I'LL ADDRESS
24 THIS TO BOTH YOU AND DR. CRUMP.
25 I MEAN, THE -- THE PART OF IT -- OF THIS
0221
01 CURVE WHICH IS RELEVANT FOR THE RISK ASSESSMENT IS NOT --
02 I MEAN, I UNDERSTAND THE CONCERNS YOU HAVE YOU ABOUT THE
03 15- TO 17-YEAR OLD GROUP, BUT THE PART THAT'S RELEVANT FOR
04 THE RISK ASSESSMENT IS REALLY THE OTHER END OF THE CURVE,
05 THE ZERO UP TO 1. -- YOU KNOW, BETWEEN THE FIRST TWO
06 POINTS, NOT THE LAST TWO POINTS.
07 AND THERE THE TWO ANALYSES PRODUCE RESULTS
08 WHICH ARE NOT TERRIBLY DIFFERENT FROM EACH OTHER, AND
09 EVEN -- EVEN PROBABLY IF YOU TOOK THE FAMOUS BLUE SLIDE
10 AND LOOKED AT THE BEGINNING PART OF THE CURVE THERE IT --
11 THAT MAY NOT EVEN BE ALL THAT DIFFERENT EITHER.
12 I MEAN, WHAT DO YOU THINK ABOUT THAT?
13 DR. GARSHICK: I THINK IF YOU'RE LOOKING FOR A
14 DOSE-RESPONSE, YOU WOULD LIKE TO INCORPORATE AS MANY
15 POINTS INTO THAT CURVE. I MEAN, YOU CAN DRAW A STRAIGHT
16 LINE BETWEEN ZERO AND 1 TO 4 OR IF THAT'S REALLY -- SOME
17 PEOPLE MAY HAVE HAD ACTUALLY 10 TO 14 YEARS IN THAT
18 GROUP.
19 SO I THINK IF YOU ARE LOOKING FOR A SLOPE,
20 YOU TRY TO INCORPORATE AS MUCH INFORMATION AS POSSIBLE.
21 DR. FROINES: KATHIE?
22 DR. CRUMP: CAN I RESPOND TO THAT? KENNY CRUMP.
23 DR. FROINES: YES, GO AHEAD.
24 DR. CRUMP: I'M DYING TO SEE THAT BLUE SLIDE. I'M
25 SORRY I WASN'T -- I WASN'T THERE.
0222
01 I THINK THE QUESTION IS -- IN MY MIND IS THAT
02 DECREASING TREND CALLS THE STUDY INTO QUESTION AND CALLS
03 WHETHER OR NOT THERE'S AN EFFECT OF DIESEL -- IT THE
04 CAUSES THE QUESTION WHETHER OR NOT THE RESPONSES YOU'RE
05 SEEING ARE REALLY RELATED TO SEE DIESEL AT ALL.
06 IF YOU ASSUME THEY ARE RELATED TO DIESEL,
07 THEN I WOULD AGREE WITH YOUR STATEMENT. IN FACT, I THINK
08 AS THE -- YOU KNOW, ANALYSIS THAT HAS BEEN CONDUCTED BY
09 CALIFORNIA SHOWS, IT DOESN'T REALLY MATTER ESSENTIALLY
10 MUCH HOW YOU DO THE ANALYSIS AS FAR AS THE SLOPE THAT YOU
11 GET.
12 BUT THE REAL QUESTION IS, IS THE -- DOES THE
13 DATA WE'RE USING, DOES IT REALLY REFLECT AN EFFECT OF
14 DIESEL AND THAT'S THE QUESTION I HAVE.
15 DR. FROINES: KATHIE AND THEN DUNCAN.
16 DR. HAMMOND: YES, I WOULD LIKE TO REMIND PEOPLE
17 THAT YEARS OF DIESEL EXHAUST EXPOSURE DOES NOT EQUAL A
18 TRUE DOSE MEASUREMENT, AND THAT IT IS ONE THING WE CAN USE
19 TO LOOK AT THIS.
20 BUT TO THE DEGREE THAT THERE IS A CHANGE IN
21 EXPOSURE OVER TIME, IF AS -- IF EXPOSURE DID DECREASE FROM
22 '59 ON, THEN YOU DON'T -- YOU'RE NOT ADDING AS MANY
23 MICROGRAMS PER CUBIC METER YEARS AS YOU ARE IN EARLIER
24 YEARS.

25 SO YOU COULD BE REALLY BE BEING MISLED, AND
0223
01 THEREFORE SAYING THAT THERE'S THIS DECREASE WITH
02 INCREASING NUMBER OF YEARS, AND THOSE INCREASING NUMBERS
03 OF YEARS MAY BE HAPPENING ENTIRELY AT THE LATER POINT.
04 YOU KNOW, CAN YOU CAN -- YOU CAN HAVE SOME REAL SKEWING OF
05 YOUR DATA.
06 SO I THINK YOU HAVE TO BE A LITTLE CAREFUL AT
07 OVERINTERPRETING SOMETHING LIKE THAT WHEN YOU'VE GOT THIS
08 CRUDER MEASURE OF EXPOSURE.
09 DR. GARSHICK: IT DOESN'T INCORPORATE INTENSITY IS
10 WHAT YOU ARE SAYING?
11 DR. HAMMOND: EXACTLY. THANK YOU.
12 DR. FROINES: OKAY. DUNCAN?
13 DR. THOMAS: I WANT TO TRY TO DRAW A LITTLE PICTURE
14 TO ILLUSTRATE THE COMPLEXITY OF TRYING TO UNDERSTAND THE
15 DIFFERENCE BETWEEN THE TWO PICTURES IN F-4 AN F -- F-2 AND
16 F-3. I'M GOING TO GO UP AND DRAW YOU A LITTLE PICTURE IN
17 A SECOND.
18 WHAT MAKES IT DIFFICULT IS THAT THE FIGURES
19 ARE NOT PROPERLY LABELED. THE LABELS ARE INCONSISTENT
20 WITH EACH OTHER, AND THEY ARE INCONSISTENT WITH WHAT'S
21 DESCRIBED IN THE TEXT.
22 SO I'M NOT EXACTLY SURE WHAT ANALYSIS
23 PRODUCED THESE TWO FIGURES, BUT LET ME SPECULATE FOR A
24 SECOND, IF YOU'LL BEAR WITH ME ONE SECOND, I WANT TO GO
25 DRAW YOU A PICTURE NOW.
0224
01 DR. FROINES: FOR THOSE OF YOU WHO MAY BE
02 WONDERING, WE'RE NOT GOING TO TAKE AN AFTERNOON BREAK.
03 WE'RE GOING TO PLUG THROUGH UNTIL 4:00 O'CLOCK ABOUT AND
04 THEN STOP. I THINK EVERYBODY WILL BE HAPPIER IF WE DO
05 THAT BECAUSE I THINK THE LAST HALF HOUR OF DISCUSSION
06 MIGHT BE LESS THAN PRODUCTIVE.
07 DR. THOMAS: THE LABEL ON THE PICTURE SAYS
08 THAT THEY ARE BASED ON COX REGRESSION USING CALENDAR YEAR
09 AS THE TIME SCALE, AND I THINK THAT APPLIES TO BOTH OF
10 THEM. AND THEN ADDITIONALLY, THERE IS CO-VARIATE
11 ADJUSTMENT FOR N-F-2, YEAR -- AGE IN 1959, AND IN F-3
12 ATTAINED AGE.
13 SO HERE'S MY RECONSTRUCTION OF IT. THERE
14 ALSO -- THE LAY MEN DOESN'T TELL ME WHICH EXPOSURE PATTERN
15 IS ASSUMED. TO KEEP THINGS -- SO THE BLOCK PATTERN. ALL
16 RIGHT. SO THAT'S EXACTLY THE PICTURE I WANTED TO DRAW.
17 SO LET'S LET THIS REPRESENT 1959. KENNY,
18 YOU'RE GOING TO HAVE TO TRY TO DECIPHER WHAT I'M SAYING
19 FROM THE DESCRIPTION. SO I'LL TRY TO DESCRIBE IT AS I'M
20 GOING.
21 DR. CRUMP: I'LL TRY TO USE MY IMAGINATION HERE.
22 DR. THOMAS: ALL RIGHT. SO WE HAVE A VERTICAL LINE
23 REPRESENTING 1959, AND NOW I'M GOING TO DRAW THE
24 TRAJECTORIES OF VARIOUS COHORT MEMBERS AS FAR AS ON THE
25 LINES, AND A TIME AXIS, WHICH IS CALENDAR YEAR.
0225
01 SO I HAVE A BUNCH OF HORIZONTAL LINES
02 REPRESENTING THE DURATIONS OF FOLLOW UP FOR VARIOUS STUDY
03 SUBJECTS, AND I'M GOING TO PUT IN A FEW X'S HERE FOR

04 DEATHS DUE TO LUNG CANCER. I'LL JUST DRAW ONE. WE HAVE A
05 LUNG CANCER AND A SECOND SUBJECT DIED HERE FOR ARGUMENT'S
06 SAKE, IN LET'S SAY IN 1970; THEREBY ACCUMULATING A MAXIMUM
07 OF 11 YEARS OF EXPOSURE.

08 NOW, SOME OF THESE PEOPLE WILL HAVE LEFT
09 EMPLOYMENT BEFORE, AND SOME WILL BE -- HAVE CONTINUED.

10 SO LET A LITTLE CIRCLE -- PUT A FEW LITTLE
11 CIRCLES HERE REPRESENTING THE AGES WHICH VARIOUS PEOPLE
12 STOPPED THEIR EXPOSURE.

13 AND I'M GOING TO DRAW ANOTHER VERTICAL LINE
14 HERE TO REPRESENT THE COX RISK SET FORMED BY THIS CASE WHO
15 DIED IN 1970.

16 AND NOW WHAT THE COX REGRESSION ANALYSIS DOES
17 IS IT COMPARES OF THE CUMULATIVE OF EXPOSURE OF THE CASE
18 WITH ALL THOSE MEMBERS OF THIS RISK SET, WHICH IN THIS
19 CASE, THIS PERSON COULDN'T SURVIVE TO ENTER THE RISK SET,
20 BUT THE OTHER PEOPLE ARE ALL THE -- FORMED THE SORT OF
21 CONTROLS AGAINST WHICH OUR CASE IS COMPARED AND BASED ON
22 THEIR CUMULATIVE EXPOSURES IN 1970.

23 NOW, THE THING TO NOTE FROM THIS COMPARISON
24 IS THAT THE CONTROLS ALL OUTLIVED THE CASE BY DEFINITION;
25 AND THEREFORE, THEY HAD THE OPPORTUNITY TO ACCUMULATE A
0226 MAXIMUM OF 11 YEARS OF EXPOSURE. NOT ALL OF THEM WOULD
02 HAVE DONE SO. HERE WE HAVE A FEW CASES THAT WILL ENTER
03 THE COMPARISON WITH LESS THAN 11 YEARS OF EXPOSURE.

04 THE CASE AS WELL COULD HAVE ACCUMULATED A
05 MAXIMUM, AND IN OUR CASE, PERHAPS, LET'S SAY NINE YEARS
06 WORTH OF EXPOSURE.

07 ALL OF THE HETEROGENEITY IN THE CASE CONTROL
08 COMPARISON HERE AT THIS RISK SET IS CONTRIBUTED BY WHEN
09 THESE PEOPLE TERMINATED EXPOSURE, AND BY THE FACT THAT THE
10 CASE THEMSELVES HAD TO HAVE TERMINATED EXPOSURE NO
11 EARLIER -- NO LATER THAN 1970 MEANS ONE MIGHT EXPECT FROM
12 THIS FORM OF ANALYSIS THAT THE CASES MIGHT GENERALLY TEND
13 TO HAVE LOWER EXPOSURES THAN THE CONTROLS.

14 NOW, THIS HIGHLIGHTS THE FUNDAMENTAL
15 COLLINEARITY PROBLEM OF THE CALENDAR YEAR AND DURATION OF
16 EXPOSURE THAT IS MOST ACCENTUATED IN THE BLOCK EXPOSURE
17 PATTERN OF ANALYSIS.

18 WHAT WE HAVE TO DO THEN IN ORDER TO GET ANY
19 REAL INFORMATION TO MAKE A MEANINGFUL COX REGRESSION
20 ANALYSIS IS TO INTRODUCE HETEROGENEITY, WHICH WE CAN DO IN
21 A NUMBER OF WAYS, ONE OF WHICH IS NOT TO ANALYZE JUST
22 YEARS OF EXPOSURE BUT TO ANALYZE CUMULATIVE DOSE, USING
23 SAY, THIS ROOF PATTERN OF EXPOSURE.

24 TO ACCUMULATE THE -- TO ALLOW FOR EXPOSURES
25 PRIOR TO 1959 WHICH WILL THEN INTRODUCE AN ADDITIONAL
0227 VARIATION HERE, TO ADOPT AGE RATHER THAN CALENDAR YEARS AS
02 THE TIME SCALE FOR PERFORMING THE RISK SETS, ANY NUMBER OF
03 THINGS WHICH WOULD LEAD TO MORE INFORMATIVE ANALYSIS.

04 BUT IT'S PRECISELY WITH THE ANALYSES OF THE
05 BLOCK EXPOSURE THAT THE COLLINEARITY PROBLEM IS MOST
06 PRONOUNCED, AND THAT'S WHY WE SHOULD NOT BE TERRIBLY
07 SURPRISED WHEN WE SEE DRAMATIC DIFFERENCES BETWEEN
08 DIFFERENT METHODS OF CONTROL OF AGE, CALENDAR YEAR WHEN

09 USING THAT EXPOSURE PATTERN.
10 THAT SAID, WE SEE --
11 DR. CRUMP: MAY I RESPOND TO THAT?
12 DR. THOMAS: SURE, BUT LET ME MAKE ONE MORE COMMENT
13 THEN I CAN GO SIT DOWN.
14 THAT WHAT WE HAVE SEEN A NUMBER OF DIFFERENT
15 ANALYSES OR PATTERNS OF DOSE-RESPONSE WHERE DOSES HERE
16 DEFINED AS DURATION OF EXPOSURE, WHICH SORT OF SEEMED TO
17 GO UP AND THEN COME BACK DOWN.
18 AND THE POINT THAT KENNY IS MAKING IS THAT IF
19 WE LOOK ONLY WITHIN THE EXPOSED WORKERS, WE GENERALLY SEE
20 NEGATIVE OFTEN -- SIGNIFICANTLY NEGATIVE WORKERS --
21 NEGATIVE DOSE-RESPONSE RELATIONSHIPS.
22 AND THIS PICTURE I'VE DESCRIBED UP HERE, WHAT
23 I MEANT TO SAY IS WE ARE LOOKING ONLY AMONGST EXPOSED
24 WORKERS. OF COURSE, WE ADD TO THIS AN EXPOSED VERSUS
25 UNEXPOSED COMPARISON. THAT'S ANOTHER WAY OF BREAKING THAT
0228
01 COLLINEARITY PROBLEM, BUT IT'S ANALYSES WHICH TREAT
02 DURATION OF EXPOSURE, USING THE BLOCK EXPOSURE PATTERN,
03 AND CALENDAR YEAR AS THE TIME SCALE AMONGST EXPOSED
04 WORKERS ONLY WHERE THIS FUNDAMENTAL COLLINEARITY PROBLEM
05 IS MOST EXTREME.
06 YOUR TURN, KENNY.
07 DR. CRUMP: I GUESS MY IMAGINATION WASN'T QUITE AS
08 GOOD AS IT SHOULD BE, BUT I THINK I HAVE AN IDEA OF WHAT
09 YOU ARE SAYING. BUT I CERTAINLY WOULD LIKE TO BE ABLE TO
10 SPEAK WITH YOU ABOUT IT AND GET A PICTURE OF -- A PICTURE
11 THAT YOU PRESENTED.
12 JUST A COUPLE OF POINTS. I DON'T -- I DIDN'T
13 DO A VERY GOOD JOB I DON'T THINK OF DESCRIBING THE
14 ANALYSIS -- OTHER ANALYSIS THAT I DID THAT WAS SEPARATE
15 FROM THE BLOCK ANALYSIS IN THAT IT WAS QUITE SIMILAR TO
16 THE RAMP ANALYSIS THAT CALIFORNIA HAS PRESENTED EXCEPT
17 THAT I ALSO USED THE DIFFERENT EXPOSURES IN THE DIFFERENT
18 GROUPS. I DIDN'T ASSUME ANYONE IS EXPOSED TO THE SAME
19 AMOUNT, AND I TOOK THE ACTUAL EXPOSURES.
20 SO THERE'S REALLY QUITE A BIT OF
21 HETEROGENEITY POSSIBLE IN THOSE DATA.
22 AND I ALSO LOOKED AT NOT JUST THE EXPOSURE
23 METHOD MEASURE USED BY CAL-E.P.A., BUT THREE OTHERS THAT
24 WE DEVELOPED. AND I DID -- I DID 16 ANALYSES USING 16
25 DIFFERENT WAYS OF -- DIFFERENT WAYS OF ACCUMULATING
0229
01 EXPOSURE, INCLUDING THE LAST FOUR YEARS, NOT INCLUDING THE
02 LAST FOUR YEARS, USING EXTERNAL CONTROLS INSTEAD OF
03 INTERNAL CONTROLS.
04 ALL 16 OF THE ANALYSES PRODUCED NEGATIVE
05 TRENDS, I THINK AND NINE OF THEM WERE STATISTICALLY
06 SIGNIFICANT, THREE OR FOUR WERE VERY HIGHLY STATISTICALLY
07 SIGNIFICANT.
08 WITH REGARD TO INCREASING YOUR HETEROGENEITY
09 BY INCLUDING THE UNEXPOSED GROUP, I THINK WHAT YOU SAY IS
10 TRUE.
11 BUT WHAT ALSO HAPPENS IS THAT YOU CAN FALSELY
12 CREATE A POLICY DOSE-RESPONSE TREND WHEN REALLY WHAT --
13 THE ONLY THING YOU'RE REALLY SEEING THERE IS THAT THE

14 EXPOSED GROUP HAS A HIGHER RISK THAN THE UNEXPOSED GROUP,
15 AND -- WHICH COULD BE FOR SOME REASON OTHER THAN DIESEL.
16 DR. FROINES: STAN?
17 DR. GLANTZ: JUST ONE OTHER QUESTION.
18 IF YOU LOOK IN ONE OF THE APPENDICES, I GUESS
19 IT'S ALSO APPENDIX F, THERE'S A TABLE IN HERE ON PAGE F-14
20 WHERE O.E.H.H.A. TRIED TO LOOK AT THE IMPORTANCE OF
21 DIFFERENCE ASSUMPTIONS THAT WERE MADE IN TERMS OF TRYING
22 TO FIGURE OUT WHY THEIR RESULTS AND DR. CRUMP'S RESULTS
23 WERE DIFFERENT.
24 AND ONE OF THE -- I WOULD LIKE TO ASK
25 DR. CRUMP JUST A COUPLE OF QUESTIONS.

0230
01 ONE IS DO YOU HAVE ANY COMMENTS ON TABLE F-1
02 IN TERMS OF WHETHER YOU AGREE WITH THEIR ASSESSMENT OF HOW
03 IMPORTANT THESE DIFFERENT ASSUMPTIONS ARE.
04 AND THE OTHER QUESTION IN MY READING OF THIS
05 IT SEEMS LIKE THE BIGGEST DIFFERENCE THAT MATTERS BETWEEN
06 THE ANALYSIS THAT STAN DAWSON DID AND THE ANALYSIS THAT
07 YOU DID IS THIS ISSUE OF WHETHER OR NOT YOU SUBTRACT OUT
08 FOR BACKGROUND.
09 AND I WAS JUST WONDERING IF YOU COULD
10 COMMENT -- IF YOU AGREE WITH MY READING OF THIS, OR IF YOU
11 HAVE SOME OTHER COMMENT ON IT?
12 DR. CRUMP: I'M -- I'M SORRY. I WOULD HAVE TO TAKE
13 TIME TO LOOK AT FIGURE F-1, AND I'LL TRY TO DO THAT AND
14 GIVE YOU PERHAPS SOME WRITTEN RESPONSE.
15 WITH REGARD TO THE SECOND POINT, I DO THINK
16 THAT IS THE IDEA THAT YOU GET WHEN YOU READ THE DOCUMENT
17 THAT THERE -- THE FACT THAT THEY SUBTRACTED OFF BACKGROUND
18 AND I DID NOT IS THE MAJOR CAUSE FOR THE DIFFERENCES IN
19 OUR ANALYSES.
20 AND I WANT TO SAY VERY CLEARLY THAT IS NOT
21 THE REASON. THE ANALYSES THAT I JUST DESCRIBED TO YOU
22 THAT PRODUCE THE NEGATIVE TRENDS, THAT COULDN'T HAVE BEEN
23 THE REASON. THE CONTROL -- THE CLERKS AND SIGNALMEN
24 WEREN'T INVOLVED IN THE ANALYSIS.
25 SO I WOULD CERTAINLY DISAGREE THAT THAT IS

0231
01 THE BASIC REASON THAT WE GET DIFFERENT RESULTS.
02 DR. BLANC: THIS IS DR. BLANC HERE.
03 IT'S -- IT'S MY IMPRESSION THAT THE ARGUMENT
04 THAT IS MADE THROUGH THIS -- THIS ANALYSIS, THIS
05 COUNTERANALYSIS THAT WE'VE BEEN DISCUSSING, JUST DOES NOT
06 SUSPEND MY DISBELIEF.
07 THERE ARE A SERIES OF CONVINCING ARGUMENTS
08 THAT THERE ARE FATAL ANALYTIC FLAWS IN THE APPROACH THAT'S
09 BEING USED, AND I FIND THOSE ARGUMENTS CONVINCING. NOT
10 ONLY THAT, TO EXTRAPOLATE FROM ONE ANALYSIS, ONE
11 ANALYTICAL APPROACH, WHICH APPEARS TO BE FATALLY FLAWED,
12 TO USE THAT AS A BASIS TO A, REJECT ENTIRELY
13 DR. GARSHICK'S WORK; AND B, THEN ON THE BASIS OF THAT,
14 REJECT ESSENTIALLY THE FINDINGS OF DR. SMITH'S
15 META-ANALYSIS; AND C, THEREFORE CONCLUDE THAT IN FACT
16 BECAUSE THERE'S NO DOSE-RESPONSE IN THIS RELATIONSHIP AND
17 BECAUSE IN -- THIS IN ANALYSIS AND BECAUSE OF THIS
18 ANALYSIS, IN FACT, EXPOSURE TO DIESEL EXHAUST IS

19 PROTECTIVE AGAINST LUNG CANCER AND ALL OTHER CAUSES OF
20 DEATH MEANS THAT THE GARSHICK DATA ARE UNBELIEVABLE AND
21 MEANS THAT IT'S NOT A CARCINOGEN.
22 IT JUST -- IT JUST IS AN UNBELIEVABLE
23 ARGUMENT, UNACCEPTABLE, UNCONVINCING, AND I BELIEVE MUST
24 BE DISREGARDED BY THIS COMMITTEE IN -- IN ITS TOTALITY.
25 DR. CRUMP: MAY I RESPOND?

0232
01 DR. BLANC: PLEASE.
02 DR. CRUMP: OKAY. WELL, I CERTAINLY AM NOT ARGUING
03 HERE THAT DIESEL IS NOT A LUNG CARCINOGEN. THAT IS NOT MY
04 ARGUMENT AT ALL.
05 MY ARGUMENT IS RESTRICTED TOTALLY TO THE
06 GARSHICK ET AL. COHORT STUDY, AND THAT'S THE -- BASICALLY
07 THE ONLY STUDY THAT I HAVE REVIEWED IN THIS DETAIL.
08 AND ALL I AM SUGGESTING IS IS THAT THE -- THE
09 PATTERN OF -- OF LUNG CANCER OR THE -- IN THIS COHORT DOES
10 NOT REFLECT DIESEL EXPOSURE.
11 I'M ALSO SUGGESTING, AND I WOULD LIKE TO
12 HAVE -- I MIGHT ASK DR. GARSHICK TO RESPOND TO THIS. I'M
13 ALSO SUGGESTING THAT I'M CONCERNED THAT THERE WAS
14 SOMETHING FUNDAMENTALLY WRONG WITH THE DATA IN THIS STUDY
15 THAT MIGHT BE CAUSING THIS.
16 AND IT COULD BE THAT IF THAT PROBLEM IS
17 CORRECTED, IF IT DOES EXIST, THAT IT MIGHT SHOW SOMETHING
18 DIFFERENT WHEN THAT PROBLEM IS CORRECTED.
19 DR. GARSHICK, DO YOU HAVE -- YOU MAY HAVE
20 COMMENTED ALREADY AND I HAVEN'T HEARD THIS ON THE STATUS
21 OF YOUR WORK TO -- TO COMPLETE THE FOLLOW UP ON THIS
22 STUDY.
23 DO YOU CARE TO COMMENT ON THAT?
24 DR. GARSHICK: WE -- I MEAN AS FAR AS WE CAN TELL
25 BASED ON THE EXPECTED RATES, IT LOOKS LIKE THE DATA ARE

0233
01 COMPLETE THROUGH 1976. I MEAN, WE -- THESE DATA WERE
02 SUPPLIED BY THE RAILROAD RETIREMENT BOARD. IN FOLLOWING
03 THAT, THEIR DEATH RECORDS BECAME INCOMPLETE, AND WE'VE
04 BEEN WORKING WITH THEM TO IDENTIFY REASONS WHY THAT WAS
05 THE CASE, AND WE THINK WE'VE GOT SOME REASONS WHY IT
06 HAPPENED.
07 SINCE THAT TIME, THEY PROVIDED US WITH AN
08 UPDATED TAPE THAT ACTUALLY HAS GONE TO H.I.C.F.A. TO HAVE
09 A CHECK -- H.I.C.F.A. BASICALLY HAS SOCIAL SECURITY FILES
10 AT THEIR DISPOSAL TO COMPARE SOCIAL SECURITY NUMBERS AND
11 LOOK FOR DEATH. AND THAT TAPE IS IN OUR HANDS, AND WE
12 HOPE TO BE LOOKING AT DEATHS AFTER 1976, BUT ARE LOOKING
13 FOR A SOURCE OF FUNDING TO FUND THAT WORK.
14 SO THAT'S THE SORTS OF THE UPDATE RIGHT NOW.
15 WE GOT THE STATUS OF THE UPDATE.
16 DR. GLANTZ: JUST TO BE CLEAR, I MEAN, YOU'RE
17 NOT -- YOU'RE STILL SAYING YOU THINK THAT THE DATA IN YOUR
18 EXISTING WORK --
19 DR. GARSHICK: RIGHT. I HAVE NO REASON TO THINK --
20 IT'S A QUESTION. ARE THE DATA BAD? I MEAN, THIS WAS A --
21 A -- RAILROAD RETIREMENT BOARD'S ADMINISTRATIVE BODY THAT
22 PAYS OUT BENEFITS TO PEOPLE AND HAS A LARGE INTEREST IN
23 MAKING SURE THEY ARE NOT PAYING TO PEOPLE WHO AREN'T

24 REALLY DEAD.
25 AND WHY DID IT HAPPEN AFTER 1977? I MEAN,
0234
01 SOME FILES DIDN'T GET UPDATED. WE'VE IDENTIFIED REASONS
02 WHY WE THINK STARTING AT THAT POINT THE DATA ARE COMPLETE.
03 SO AS FAR AS WE KNOW, THESE ARE THE DATA, AND
04 I CAN'T EXPLAIN ANY -- THIS IS JUST THE WAY IT IS.
05 DR. GLANTZ: YEAH, OKAY.
06 DR. GARSHICK: I MEAN, I CAN'T ANSWER THE QUESTION
07 DIRECTLY. I MEAN, WE CERTAINLY DIDN'T DO ANYTHING TO THE
08 DATA TO MAKE IT BAD. THIS IS IT.
09 DR. GLANTZ: BUT I MEAN, AS FAR AS -- AS FAR AS YOU
10 CAN TELL THAT YOU WERE WORKING WITH -- EXCEPT FOR THE
11 PROBLEMS YOU'VE IDENTIFIED WITH IT, WITH A GOOD DATA SET
12 AS FAR AS YOU COULD TELL?
13 DR. GARSHICK: AND THE ENTIRE DATA BASE HAS BEEN
14 SENT TO H.I.C.F.A. TO BE MATCHED THROUGH H.I.C.F.A. MATCH
15 TO LOOK FOR MISSING DEATHS, IF YOU WOULD.
16 SO WE'RE TRYING TO CORRECT ANY POTENTIAL
17 PROBLEM, EVEN IN TIMES 1976 AND BEFORE.
18 DR. FROINES: I HAVE NO COMMENT. I -- I KNOW
19 ENOUGH WHEN YOU MAKE PENETRATING QUESTIONS TO KNOW WHEN TO
20 NOT FOLLOW THEM UP WITH THINGS THAT AREN'T AS GOOD.
21 SO I THINK THAT THE POINT IS THAT PAUL'S
22 COMMENTS ARE QUITE GERMANE, ESPECIALLY SINCE ERIC IS HERE
23 AND TOM SMITH WAS HERE AND KATHIE HAMMOND WAS HERE, AND I
24 TALKED WITH DOUG DOCKERY ABOUT THIS WORK NOT LONG AGO.
25 IT -- AN AWFUL LOT OF VERY DISTINGUISHED
0235
01 SCIENTISTS WOULD BE AWFULLY WRONG IF THERE WAS A
02 FUNDAMENTAL FLAW IN THIS DATA, WHICH IS NOT TO SUGGEST
03 THERE AREN'T UNCERTAINTIES THAT NEED TO BE ADDRESSED.
04 AND I THINK THAT WE WOULD ALL AGREE THAT
05 ADDITIONAL RESEARCH TO HELP CLARIFY SOME OF THESE
06 QUESTIONS IS -- IS IMPORTANT, AND I THINK FOLLOW UP FOR
07 ERIC TO FIND FUNDS TO FOLLOW UP I THINK IS REALLY QUITE
08 IMPORTANT AND SO THAT -- BUT I THINK THAT I WOULD TEND TO
09 AGREE WITH PAUL THAT ONE WOULD HAVE TO FIND SOME VERY
10 CONVINCING REASONS TO SUGGEST THAT THIS ENTIRE STUDY IS
11 FUNDAMENTALLY FLAWED.
12 DR. DAWSON: I WOULD JUST LIKE TO TALK ABOUT MY
13 IMPRESSION OF THE SITUATION WITH REGARD TO THE SUBTRACTION
14 OF BACKGROUND.
15 NOW, WHAT -- WHAT I DID LAST SPRING, I THINK
16 IT WAS, WAS TO DO A RUN, WHICH AS NEARLY AS POSSIBLE COULD
17 REPLICATE DR. CRUMP'S WORK. AND ALSO MY OWN WORK, EXCEPT
18 THAT I -- I SUBTRACTED BACKGROUND SO THAT I HAD A DIRECT
19 COMPARISON, AS DIRECT AS I KNEW HOW TO DO OF HIS APPROACH
20 AND MINE.
21 AND ESSENTIALLY THE -- THE RESULTS VERIFIED
22 THAT DR. CRUMP GOT SOME INSIGNIFICANT SLOPES, AND I GOT
23 SIGNIFICANT SLOPES WHEN I -- YOU KNOW, WHEN HE DIDN'T
24 SUBTRACT BACKGROUND, THE SLOPES WERE INSIGNIFICANT, AND
25 WHEN I -- MOSTLY. AND WHEN I DID THEY WERE SIGNIFICANT
0236
01 MOSTLY.
02 AND SO THAT'S ONE OF THE REASONS WHY THE

03 REPORT STRESSES THIS POINT THAT THE DIFFERENCE BETWEEN
04 THIS IS THAT ISSUE.
05 DR. FROINES: KATHIE?
06 DR. CRUMP: CAN I RESPOND --
07 DR. HAMMOND: I THINK -- LET ME JUST SAY SOMETHING
08 ABOUT -- THERE'S TWO KINDS OF BACKGROUNDS HERE IN
09 SUBTRACTING, AND I THINK IT'S IMPORTANT TO DISTINGUISH
10 THOSE.
11 I THINK THAT SUBTRACTING BACKGROUNDS OF THE
12 TRAIN CREW IS ONE THING, AND THEN AS FAR AS I'M
13 CONCERNED -- AND THOSE OF US THAT DO THE EXPOSURE
14 ASSESSMENT, THAT THE CLERK SHOULD BE CONSIDERED UNEXPOSED.
15 SO YOU DON'T SUBTRACT THE SAME KIND OF NUMBER
16 BACKGROUND. YOU SET THAT -- AND I THINK THIS IS WHAT YOU
17 DID -- YOU SET THAT TO ZERO. BUT IT'S NOT A SUBTRACTING
18 BACKGROUND. IT'S SETTING THE CLERK'S EXPOSURE TO ZERO
19 BECAUSE THAT'S WHAT IT IS.
20 DR. DAWSON: YEAH. THAT -- THAT'S --
21 DR. HAMMOND: THE TRAIN --
22 DR. DAWSON: THAT'S ESSENTIALLY IT, THAT YOU'RE
23 ZEROING THE CLERK'S EXPOSURE ON THE BASIS THAT THEY WERE
24 UNEXPOSED TO DIESEL EXHAUST, AND THEN -- AND THEN IN OUR
25 CASE, WE SUBTRACTED THEIR VALUE FROM THE TRAIN WORKERS.
0237
01 DR. HAMMOND: RIGHT.
02 DR. DAWSON: AND YOU'VE SUGGESTED ANOTHER WAY TO DO
03 THAT WHICH IS FINE.
04 AND TO ME, THIS TESTS THE HYPOTHESIS THAT
05 DIESEL EXHAUST IS A CARCINOGEN; WHEREAS IF YOU DON'T DO
06 THAT, IT TESTS ANOTHER HYPOTHESIS THAT R.S.P. E.T.S.
07 ADJUSTED R.S.P. IS A CARCINOGEN.
08 DR. CRUMP: MAY I RESPOND TO THAT?
09 DR. FROINES: SURE, SORRY. I DIDN'T MEAN -- I WAS
10 SAYING SOMETHING TO STAN.
11 DR. CRUMP: I'M SORRY. WAS HE -- I DIDN'T BUTT IN,
12 DID I?
13 DR. FROINES: NO, NO. YOU'RE FINE.
14 DR. CRUMP: OKAY. WELL, AS I SAID OTHER TIMES
15 ALREADY TODAY, IT JUST SO HAPPENS THAT WHEN YOU DO IT THE
16 WAY STAN DESCRIBED, AND YOU ASSIGN ZERO EXPOSURES TO
17 THE -- CLERKS, BASICALLY ALL OF YOUR ANALYSES ARE
18 COMPARING CLERKS TO TRAINRIDERS.
19 AND IF THE TRAIN RIDERS HAD A HIGHER
20 INCIDENCE OF CANCER -- MORTALITY FROM CANCER, LUNG CANCER,
21 WHICH THEY DID, THEN VIRTUALLY WITH ANY SORT OF
22 DOSE-RESPONSE ANALYSIS, THE ANALYSIS THAT STAN DESCRIBED
23 WOULD GIVE YOU A SIGNIFICANT L.M.U. TREND.
24 AND WHEN YOU CAN SEE THAT BY LOOKING AT
25 FIGURE F-3 THAT WE -- THAT WE'VE TALKED ABOUT, THAT SHOWS
0238
01 THAT A DECREASING TREND; BUT YET ANALYSIS THAT STAN
02 DESCRIBES GIVES YOU A POSITIVE SLOPE.
03 OF COURSE, IT GIVES YOU EXTREMELY -- A BAD
04 FIT TO THE DATA, BUT IT DOES GIVE YOU A POSITIVE SLOPE.
05 SO I'M SUGGESTING YOU CAN'T JUST LOOK AND SEE
06 IF A SLOPE IS POSITIVE OR NOT. YOU HAVE TO LOOK AND SEE,
07 I THINK, IF THERE IS A -- IF THE DOSE-RESPONSE TREND

08 YOU'RE GETTING IS A BIOLOGICALLY PLAUSIBLE.
09 DR. FROINES: I -- I DON'T UNDERSTAND THAT LAST
10 SENTENCE.
11 DR. CRUMP: THE TRENDS -- FOR EXAMPLE, YOU SEE IN
12 F-3. YOU SEE A -- AS THE SHOP -- AS THE TRAIN RIDERS WERE
13 EXPOSED, THE TRAIN RIDERS THAT WERE EXPOSED TO THE LEAST
14 OR THE SHORTEST -- SHORTEST AMOUNT OF TIME OR TO THE LEAST
15 AMOUNT OF DIESEL HAD THE HIGHEST RELATIVE RISK OF LUNG
16 CANCER.
17 AND AS THAT EXPOSURE INCREASED OR THE
18 DURATION OF EXPOSURE INCREASED, THEIR RISK OF LUNG CANCER
19 DECREASED, IT DID NOT INCREASE. THAT IS NOT A BIOLOGICAL
20 PLAUSIBLE EFFECT OF DIESEL EXPOSURE.
21 THERE -- IT DOESN'T SHOW THE DOSE-RESPONSE
22 TREND YOU WOULD EXPECT IF DIESEL WERE CAUSING THIS TREND
23 TO OCCUR.
24 DR. FROINES: WELL, THAT'S BEEN DISCUSSED AT SOME
25 LENGTH EARLIER WHEN I THINK YOU WEREN'T ON, AND WE'LL HAVE
0239
01 TO MAKE SURE YOU HAVE THE TRANSCRIPT ON THAT.
02 I DON'T THINK THERE'S MORE THAT CAN BE SAID
03 ABOUT THAT RIGHT NOW.
04 KATHIE?
05 DR. HAMMOND: AND CHANGE THE SUBJECT, IS THAT
06 OKAY?
07 A POINT THAT HASN'T BEEN DISCUSSED TODAY
08 HAS -- IS THE ISSUE -- IT'S TRUE THAT THE COMPARISON,
09 GENERALLY SPEAKING, IS TRAIN CREW TO CLERKS, AND I WOULD
10 LIKE TO REMIND PEOPLE THAT I THINK THERE AN UNDERLYING
11 NEGATIVE CONFOUNDER IN THAT COMPARISON. AND THAT IS THE
12 CLERKS HAVE A HIGH EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE
13 COMPARED TO THE TRAIN CREW.
14 AND TO THE DEGREE THAT ENVIRONMENTAL TOBACCO
15 SMOKE CAUSES LUNG CANCER, YOU ARE COMPARING THE RATE OF
16 THE TRAIN CREW'S LUNG CANCER TO AN ALREADY ELEVATED RATE.
17 SO THE TRUE ELEVATED RATE IS EVEN HIGHER.
18 DR. FROINES: GOOD POINT.
19 DR. HAMMOND: AND WHETHER OR NOT YOU WANT TO DO
20 ANYTHING ABOUT THAT AT THIS POINT -- THIS MAY BE A LATE
21 DATE TO DO ANYTHING ABOUT THAT, BUT I WOULD JUST LIKE TO
22 POINT OUT FROM THAT PERSPECTIVE THIS -- ALL THIS WORK IN
23 THIS ANALYSIS REPRESENTS AN UNDERESTIMATE OF THE POTENCY
24 OF DIESEL EXHAUST.
25 DR. FROINES: CAN I SUGGEST THAT PETER TALK?
0240
01 DR. WITSCHI: I HAVE A QUESTION AND IT'S TO ERIC
02 AND MAYBE I HAVE MISSED IT, YOU KNOW.
03 THERE IS YOUR LETTER WHEN YOU CAME DOWN IN
04 WRITING THAT YOU OBJECT TO USING YOUR STUDIES FOR A
05 QUANTITATIVE RISK ASSESSMENT, AND I'M NOT QUITE CLEAR
06 TODAY WHERE WE STAND ON THAT ONE.
07 COULD YOU CLARIFY THIS FOR ME?
08 DR. GARSHICK: WELL, I THINK THE ISSUE WAS THAT
09 TRYING TO HAVE ONE SLOPE DESCRIBE ALL THE DATA AT THIS
10 POINT IS -- HAS MANY UNCERTAINTIES, AND THAT REALLY IS THE
11 MAJOR OBJECTION.
12 AND I THINK THAT, YOU KNOW, TRYING TO

13 EXTRAPOLATE BACK PAST EXPOSURES PLUS WITH THE STUDY THAT
14 NEEDS SOME ADDITIONAL FOLLOW UP TO DEFINE THAT SLOPE, AND
15 THAT WAS REALLY -- REALLY MY POINT.
16 AND I MEAN, IT SHOULDN'T BE UNDO EMPHASIS --
17 THERE SHOULDN'T BE UNDUE EMPHASIS PUT ON THE SLOPE,
18 PARTICULARLY GIVEN THE DISCUSSIONS WE'RE HAVING RIGHT
19 NOW.
20 AND I -- I THINK THAT IT DEPENDS ON WHAT'S
21 DRIVING THE PROCESS. I MEAN, IF -- IF THE LAW SAYS THE
22 CALIFORNIA MUST COME UP WITH A -- WITH A SLOPE TO DRIVE
23 REGULATION, THEN THE POTENTIAL PROBLEM, POINTING AN
24 EMPHASIS ON THAT SLOPE, GIVEN ALL THE UNCERTAINTY -- ON
25 THE OTHER HAND, THE BOARD HAS TO IDENTIFY A TOXIC AIR
0241 CONTAMINANT BASED ON QUALITATIVE DISCUSSION, THEN WE HAVE
02 DONE THAT.
03 DR. GLANTZ: WELL, SEE THOUGH, I THINK YOU'RE KIND
04 OF MIXING -- YOU'RE KIND OF MIXING UP TWO POINTS HERE.
05 I THINK ONE QUESTION IS THE FUNDAMENTAL
06 QUALITY OF THE DATA, AND I THINK YOU'VE DEFENDED THAT
07 PRETTY WELL AT THIS MEETING TODAY.
08 THE SECOND QUESTION IS WHAT MODEL OR
09 MATHEMATICAL FUNCTION SHOULD YOU HAVE USED TO TRY TO
10 EXTRACT SOME SORT OF RISK NUMBER FROM THE DATA.
11 DR. GARSHICK: RIGHT.
12 DR. GLANTZ: AND I MEAN, WHAT YOU WERE ARGUING
13 EARLIER WITH THE INFAMOUS BLUE SLIDE WAS DON'T JUST DRAW
14 ONE STRAIGHT LINE IN CERTAIN WAYS.
15 BUT I THINK -- OR LET ME ASK YOU THIS. WOULD
16 IT BE FAIR TO SAY THAT YOUR DATA, APPROPRIATELY ANALYZED,
17 WHATEVER THAT MEANS, WOULD BE SUITABLE IN FACT FOR DOING
18 THE RISK ASSESSMENT? IT'S NOT A PROBLEM WITH THE DATA
19 ITSELF --
20 DR. GARSHICK: THAT'S RIGHT. I DON'T THINK IT'S A
21 PROBLEM WITH THE DATA. IT'S A PROBLEM RIGHT NOW, I
22 MEAN, -- I TRIED TO IDENTIFY TWO THINGS WE CAN DO TO
23 IMPROVE THAT, AND WHEN THAT SHOULD BE DONE I'M NOT SURE.
24 THAT'S UP TO THE COMMITTEE.
25 BUT THE ONE IS THE FOLLOW UP, AND ONE IS
0242 GOING BACK AND TRYING TO REALLY NAIL DOWN WHEN THOSE
02 PEOPLE STARTED BEING EXPOSED TO DIESEL BECAUSE IT WASN'T
03 THE START OF FOLLOW UP -- THE START OF EXPOSURE IS VERY
04 IMPORTANT AND WHAT THE LEVELS MIGHT HAVE BEEN, AND WE ARE
05 ATTEMPTING TO DO THAT.
06 DR. GLANTZ: BUT YOU WERE -- I THINK THAT -- AND I
07 THINK ACTUALLY THIS HAS BEEN A CLARIFYING DISCUSSION FOR
08 ME BECAUSE, I MEAN, I THINK THE COMMENTS THAT YOU'VE
09 SUBMITTED EARLIER WERE BEING INTERPRETED AS SAYING, WELL,
10 THERE WAS SOMETHING WRONG WITH THIS DATA --
11 DR. GARSHICK: NO.
12 DR. GLANTZ: NO. I UNDERSTAND WHAT YOU'RE SAYING
13 NOW. THAT IS VERY HELPFUL.
14 DR. FROINES: GEORGE?
15 DR. ALEXEEFF: AS A CLARIFYING POINT, AND YOU CAN
16 INDICATE WHETHER OR NOT THIS IS THE CASE.
17 I THINK ONE OF THE ISSUES THAT YOU HAD WAS US

18 USING THE ORIGINAL PUBLISHED SLOPE THAT CAME FROM YOUR
19 STUDY AS OPPOSED TO THE OTHER ORIGINAL DATA ANALYSIS THAT
20 YOU HAD. I MEAN THAT WAS ONE ISSUE THAT --
21 DR. GARSHICK: THAT WAS EARLY ON. I THINK THAT --
22 THAT WAS DONE -- RIGHT. I THINK THAT WE'VE SETTLED THAT
23 ISSUE, BUT THERE'S BEEN A CONSIDERABLE ANALYSIS ON THE
24 DATA SET. YOU KNOW, EVEN NOT INCORPORATING FOLLOW UP
25 AFTER 1976.

0243

01 AND I'VE -- ALL I TRIED DO WAS MAKE PEOPLE
02 AWARE OF THE LIMITATIONS AND SO HAS TOM. I MEAN, TOM SAID
03 HE DIDN'T THINK IT WAS POSSIBLE.

04 NOW, I THINK WE NEED TO GO BACK AND TRY TO
05 BETTER DEFINE HISTORICAL RAILROAD EXPOSURES, JUST GREAT
06 UNCERTAINTY ASSIGNED TO ONE SLOPE LOOKING AT THESE DATA.

07 DR. FROINES: I DON'T KNOW IF THAT IS TRUE. I
08 THINK THAT WHEN YOU GO THROUGH AND YOU LOOK AT WHAT'S BEEN
09 DONE IN THIS DOCUMENT AND LOOK AT THE RANGE OF RISK THAT
10 PEOPLE HAVE IDENTIFIED, AS I LOOK AT THE NUMBERS IN THE
11 ANALYSIS AND THE CONCLUSIONS, IT SEEMS TO ME, THAT THAT
12 RANGE IS FAIRLY REASONABLE HAVING BEEN LOOKED AT IN A
13 NUMBER OF DIFFERENT WAYS.

14 AND THAT WITHIN THE LIMITS OF -- OF SOME
15 OTHER DISCUSSIONS AND GIVEN THE LIMITS OF YOUR DATA, THAT
16 THESE GUYS SEEM PRETTY SOLID TO ME, AND THAT WE DO HAVE
17 UNCERTAINTY ABOUT THOSE NUMBERS. THERE'S NO QUESTION
18 ABOUT IT, AND I DON'T THINK ANYBODY IN THIS ROOM WOULD
19 ARGUE THAT.

20 BUT I THINK THAT THE DATA IS LEGITIMATE FOR
21 USE AND -- AND WHAT STAN AND OTHERS HAVE DONE HAVE BEEN --
22 IN FACT, GONE TO GREAT ENDS.

23 WE HAVE NEVER EVER HAD A DOCUMENT -- IN FACT,
24 YOU COULD TAKE EVERY RISK ASSESSMENT WE'VE EVER DONE AND
25 COMBINE THEM TOGETHER, AND THEY WOULDN'T MAKE THE DEPTH OF

0244

01 THIS RISK ASSESSMENT.

02 AND I THINK THAT ONE HAS TO PUT THIS RISK
03 ASSESSMENT INTO SOME PERSPECTIVE. WE'VE HAD -- THIS IS
04 NOW OUR THIRD WORKSHOP. WE HAVE GONE THROUGH THIS AND
05 THROUGH IT AND THROUGH IT, AND WE WILL NEVER, I HOPE IN MY
06 LIFE AGAIN, HAVE TO GO THROUGH A CHEMICAL OF THIS WITHIN
07 THIS DEPTH.

08 AND SO THAT AT SOME LEVEL WE ARE SAYING THAT
09 WE HAVE AN ENORMOUS AMOUNT OF DATA THAT WE'RE USING, AND
10 WE'RE PENALIZING OURSELVES BY CONTINUING TO -- IN A SENSE,
11 ALMOST OVERSTATE THE UNCERTAINTY, WHICH ISN'T TO SAY THERE
12 ISN'T AN ENORMOUS AMOUNT OF WORK LEFT TO BE DONE BECAUSE
13 THERE CLEARLY IS, AND HOPEFULLY YOU WILL DO MUCH OF IT.
14 AND THERE ARE CLEARLY BIOLOGICAL ISSUES THAT NEED FURTHER
15 DETERMINATION. NOBODY IS ARGUING THAT THIS IS A CLOSED
16 BOOK.

17 BUT I ALSO THINK THAT WE SHOULD BE --
18 SHOULDN'T BE HESITANT TO SAY THERE IS AN AWFUL LOT THERE
19 AS WELL AND THAT WE CAN USE THAT TO MAKE SOME DECISIONS TO
20 HELP US GO FORWARD, RECOGNIZING THOSE -- RECOGNIZING THOSE
21 UNCERTAINTIES.

22 I MEAN, I HATE TO BRING THIS BACK, BUT WHEN

23 WE DID METHYLENE CHLORIDE A FEW YEARS AGO, WE TOOK THREE
24 DATA SETS. AN ANIMAL STUDY AT 4,000, 2,000 AND A CONTROL,
25 AND WE DREW A LINE THROUGH IT, AND WE SAID THAT'S IT. AND
0245

01 THAT WAS IT. AND BY THESE STANDARDS, THAT WAS SILLY AT
02 BEST.

03 AND THEN DALE AND SOME OTHERS CAME IN AND
04 SAID, OH, WE'VE GOT TO MAKE A LITTLE ADJUSTMENT BECAUSE
05 WE'VE GOT SOME COMPETITION BETWEEN P-450 AND GLUTATHIONE
06 AND, SO WE DID SOME P.B.P.K. MODELING, AND THAT WORKED OUT
07 FINE.

08 AND SO ONE HAS TO HAVE SOME HUMILITY ABOUT
09 THE SCOPE OF THIS DATA. I THINK ACTUALLY WE'RE DEALING
10 WITH OVER 30 EPIDEMIOLOGIC STUDIES, AND THAT THE DATA WE
11 HAVE BEFORE US IS ACTUALLY QUITE GOOD. WE SHOULD SAY
12 THAT. IT IS QUITE GOOD, AND WE HAVE DONE AN AWFUL LOT OF
13 WORK IN THE PROCESS.

14 NOW, I DON'T KNOW HOW THIS PANEL IS GOING TO
15 DECIDE IN A MONTH FROM NOW, BUT I CERTAINLY DON'T AGREE
16 WITH THE NOTION THAT THE DATA IS FUNDAMENTALLY FLAWED AND
17 THERE ARE SO MANY UNCERTAINTIES THAT WE CAN'T FIND OUR WAY
18 THROUGH THE -- FROM THE FOREST TO THE TREES OR VICE VERSA.
19 ANYWAY.

20 DR. GARSHICK: YOU KNOW, IN TERMS OF THE
21 QUANTITATIVE ASPECTS OF THE ANALYSIS, IN TERMS OF THE
22 QUALITATIVE ASPECTS, A LOT OF -- A LOT OF WEIGHT TENDS TO
23 BE GIVEN TO DECISIONS MADE BY -- BY BODIES SUCH AS THIS,
24 PARTICULARLY SPECIFYING RANGES SUCH AS UPPER LEVELS OF
25 RANGE MAY BE UNDULY EMPHASIZED AS COMPARED TO LOW LEVELS
0246

01 OF RANGES. AND THAT'S WHAT I'M TALKING ABOUT, THE
02 UNCERTAINTY.

03 NOW, IT SHOULDN'T -- IT SHOULDN'T PARALYZE
04 THE REGULATORY PROCESS, BUT AND THE REASON WHY I'M
05 EMPHASIZING THE UNCERTAINTIES IS THAT MAY INDEED HAPPEN,
06 AND UNTIL WE KNOW MORE ABOUT THE ACTUAL POTENCY OF DIESEL
07 PER SE, WE'LL BE FORCED TO LIVE WITH THE -- HAVE THE
08 UNCERTAINTIES, AND I THINK THAT THE STAFF MADE A COMMENT
09 THAT THEIR OPINION THAT THE LOWER LEVEL OF THE RANGE WAS
10 MORE -- MORE APPROPRIATE. PERHAPS LOWER THAN THAT.

11 SO I THINK THAT'S THAT -- I'LL JUST ADD THAT
12 CAVEAT.

13 DR. FROINES: I AGREE. I AGREE. NO PROBLEM. NO
14 PROBLEM.

15 I THINK THAT -- LET ME -- LET ME ASK YOU A
16 COUPLE OF QUESTIONS. ACTION ITEMS. WE SHOULD ALWAYS HAVE
17 ACTION ITEMS AFTER A MEETING. ONE ACTION ITEM -- WHAT?

18 DR. GLANTZ: ADJOURNING.

19 DR. FROINES: I UNDERSTAND THAT, AND IF I DON'T
20 SHUT UP AND -- ERIC AND I SHUT UP SOON, THERE WON'T BE
21 ANYBODY TO TALK ABOUT ACTION ITEMS WITH BECAUSE A NUMBER
22 OF PEOPLE HAVE LEFT ALREADY.

23 BUT FIRST IS THOSE PEOPLE WHO HAD SLIDES OR
24 OVERHEADS, WE DO NEED TO GET -- OBTAIN THEM SO WE CAN SEND
25 COPIES OF THE SLIDES AND OVERHEADS TO ALL THE ATTENDEES.
0247

01 SO THAT'S ONE ACTION ITEM.

02 NOW, THE ONLY OTHER QUESTION I HAVE, AND I
03 WILL STOP FOR THE DAY IS DOES THE PANEL HAVE ANY COMMENTS
04 ABOUT ANYTHING THAT WE BILL LOCKETT, MYSELF, AND GEORGE
05 SHOULD BE DOING OVER THE NEXT MONTH BEFORE WE HAVE THE --
06 THE PREMIERE MEETING.

07 DR. WITSCHI: YEAH. I WOULD MENTION, AGAIN, I
08 WOULD LIKE YOU TO TALK TO ALLAN SMITH SO HE CAN GET
09 SOMETHING TO US IN WRITING WHAT HIS ASSUMPTIONS WERE AND
10 WHAT HIS PROCEDURES WERE FOR US TO COME TO THIS ESTIMATE
11 ABOUT AND TWO AND ONE THOUSAND. I THINK I REALLY WOULD
12 NEED SOME DOCUMENTATION ON THAT ONE.

13 DR. FROINES: AND I -- BILL, I WOULD REALLY VERY
14 MUCH LIKE TO GET A COPY OF THE TRANSCRIPT TO EVERYBODY AND
15 I -- AND I HOPE YOU WOULD BE WILLING TO TAKE THE
16 TRANSCRIPT BECAUSE -- AND I THINK KENNY AND TOM SMITH
17 ESPECIALLY -- SO THAT IF ANYBODY WANTS TO MAKE COMMENTS
18 BASED ON WHAT THEY HAVE IN THE TRANSCRIPT, TO CLARIFY
19 THINGS, TO BRING -- TO SAY SOMETHING FURTHER THAT THEY
20 HAVE THAT OPPORTUNITY.

21 SO THAT -- SO THAT EVERYBODY COMES AWAY
22 FEELING THAT THAT THE PROCESS HAS BEEN A COMPLETELY OPEN
23 ONE, AND THEY'VE HAD A COMPLETE -- HAD ABILITY TO
24 COMMUNICATE CONCERNS THAT MAY HAVE NOT BEEN EXPRESSED
25 HERE.

0248

01 ANYTHING ELSE? WE'RE ADJOURNED. THANK YOU
02 VERY MUCH.

03 THANK YOU VERY MUCH FOLKS THAT CAME AS
04 INVITED GUESTS. AND FOR THOSE PEOPLE IN THE AUDIENCE THAT
05 NEVER GOT ANY CHANCE TO ASK A QUESTION, I APOLOGIZE, BUT
06 YOU'RE MORE THAN WELCOME TO SEND ME TO ME IN WRITING.

07 (END OF PROCEEDINGS)

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